FIG. 1

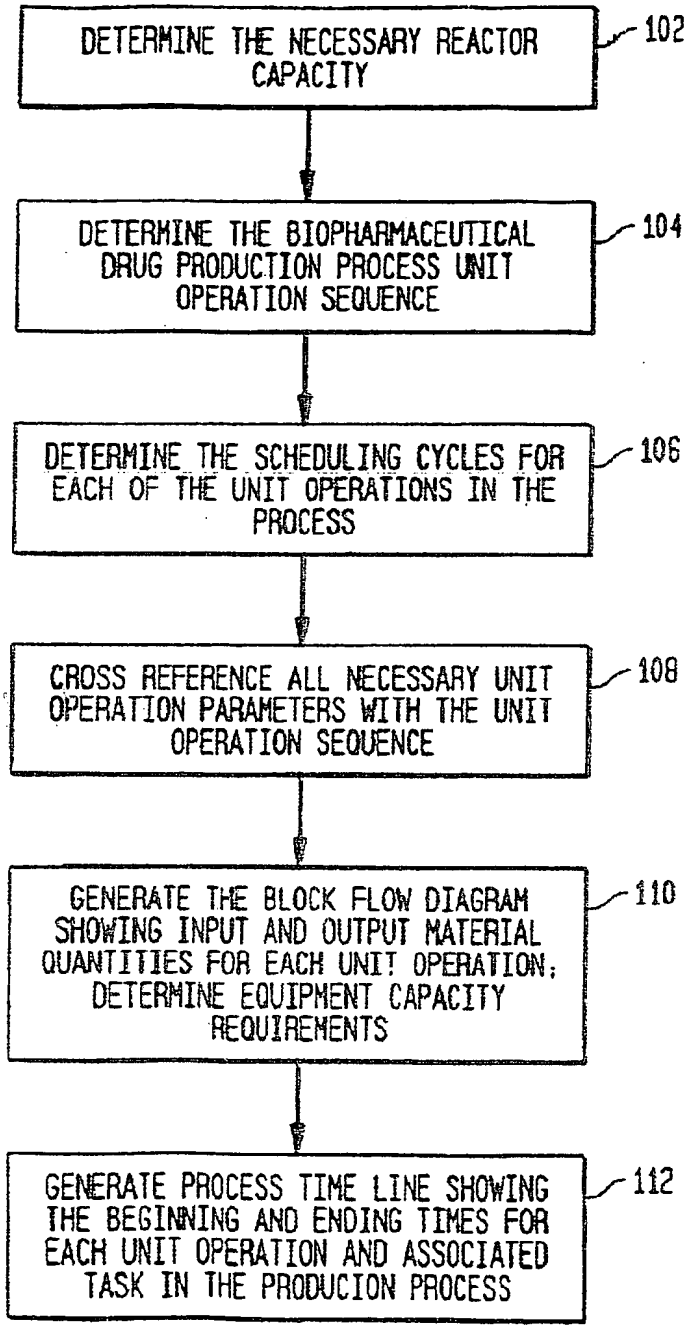

DETERMINE THE NECESSARY REACTOR CAPACITY
102
DETERMINE THE BIOPHARMACEUTICAL DRUG PRODUCTION PROCESS UNIT OPERATION SEQUENCE
104
DETERMINE THE SCHEDULING CYCLES FOR EACH OF THE UNIT OPERATIONS IN THE PROCESS
106
CROSS REFERENCE ALL NECESSARY UNIT OPERATION PARAMETERS WITH THE UNIT OPERATION SEQUENCE
108
GENERATE THE BLOCK FLOW DIAGRAM SHOWING INPUT AND OUTPUT MATERIAL QUANTITIES FOR EACH UNIT OPERATION; DETERMINE EQUIPMENT CAPACITY REQUIREMENTS
110
GENERATE PROCESS TIME LINE SHOWING THE BEGINNING AND ENDING TIMES FOR EACH UNIT OPERATION AND ASSOCIATED TASK IN THE PRODUCION PROCESS
112

FIG. 2

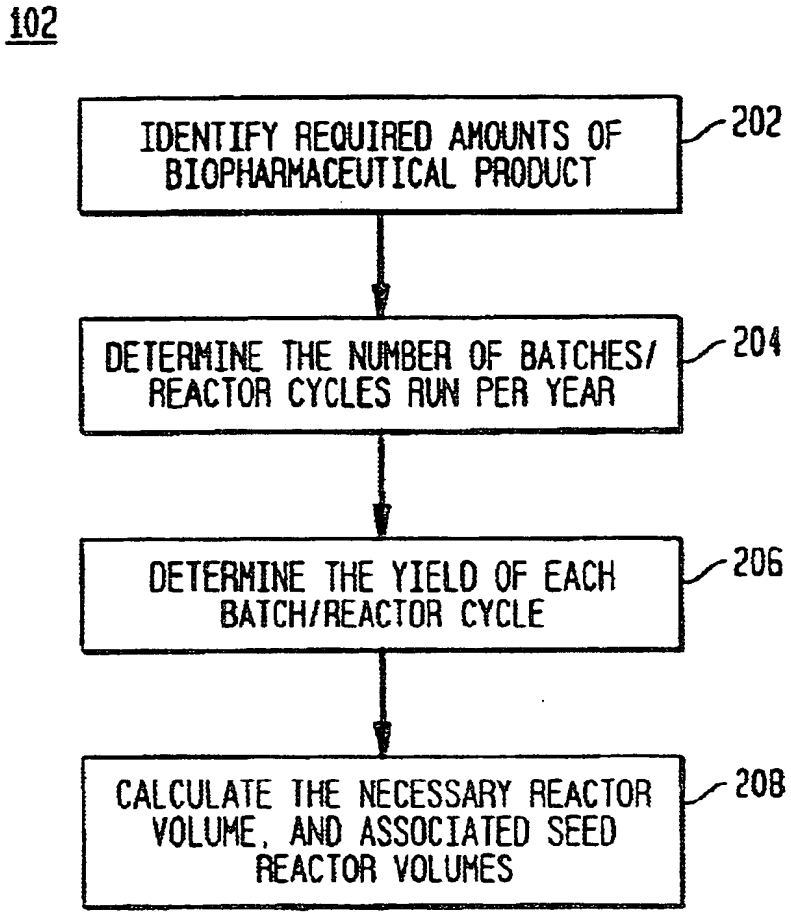

102
IDENTIFY REQUIRED AMOUNTS OF BIOPHARMACEUTICAL PRODUCT
202
DETERMINE THE NUMBER OF BATCHES/ REACTOR CYCLES RUN PER YEAR
204
DETERMINE THE YIELD OF EACH BATCH/REACTOR CYCLE
206
CALCULATE THE NECESSARY REACTOR VOLUME, AND ASSOCIATED SEED REACTOR VOLUMES
208

FIG. 3
UNIT OPERATIONS LIST

MICROBIAL FERMENTATION PROCESS

UOP SEQ. NO.	CODE	UNIT OPERATION TYPE	CYCLES PER UnOp OFFSET (HRS)	CYCLES PER BATCH UnOp START	CYCLES PER BATCH UnOp END	CYCLES PER BATCH OFFSET (HRS)	PROCESS UnOp START	PROCESS UnOp END	PROCESS OFFSET (HRS)	RECOVERY PRODUCT SWR	RECOVERY PRODUCT OAR	RECOVERY TOTAL PROTEIN SWR	RECOVERY TOTAL PROTEIN OAR
1	1	INOCULUM PREP	1	3	6	1	1						
2	2	FLASK GROWTH	1	3	6	1	1						
3	53	SEED FERMENTATION	1	3	6	1	1						
4	3	PRODUCTION FERMENTATION	1	3	6	1	1			100%	100%	100%	100%
5	51	HEAT EXCHANGE	1	3	6	1	1			100%	100%	100%	100%
6	28	CONT. CENTRIFUGATION/WHOLE CELL HARVEST	1	3	6	1	1			95%	95%	95%	95%
7	48	RESUSPEND CELL PASTE	1	1			1			100%	95%	100%	95%
8	51	HEAT EXCHANGE	1	3	8	10	1			100%	95%	100%	95%
9	31	CELL DISRUPTION/HIGH PRESSURE	1	3	8	10	1			80%	76%	90%	86%
10	51	HEAT EXCHANGE	1	3	8	10	1			100%	76%	100%	86%
11	48	RESUSPENSION/SURFACTANT	1	2	11	12	1			100%	76%	95%	81%
12	29	CONT. CENTRIFUGATION/PRECIPITATE HARVEST	1	2	11	12	1			95%	72%	32%	26%
13	48	RESUSPENSION/BUFFER	1	1			1			100%	72%	95%	24%
14	29	ULTRAFILTRATION/CONCENTRATION/DILUTION	1	1			1			95%	68%	95%	23%
15	48	MICROFILTRATION/TANGENTIAL FLOW	1	1			1			93%	64%	95%	22%
16	36	PRODUCT ADSORPTION HPLC	1	1			1			85%	54%	33%	7%
17	34	PRODUCT ADSORPTION HPLC	1	1			1			90%	49%	40%	3%
18	39	ULTRAFILTRATION/FLOW DIALYSIS	1	1			1			95%	46%	95%	3%
19	39	PRODUCT ADSORPTION HPLC	1	1			1			85%	39%	55%	2%
20	37	ULTRAFILTRATION/FLOW DIALYSIS	1	1			1			90%	35%	95%	1%
21	39	PRODUCT ADSORPTION HPLC	1	1			1			90%	32%	80%	1%
22	37	MICROFILTRATION/DEAD END	1	1			1			95%	30%	95%	1%
23	99	END											

302 304 306 308 310 312 314 316 318 320 322 324 326 328 330 332

FIG. 4
UNIT OPERATIONS LIST

MAMMALIAN CELL CULTURE PROCESS

UOP SEQ. NO.	CODE	UNIT OPERATION TYPE	CYCLES PER UnOp OFFSET (HRS)	CYCLES PER BATCH UnOp START	CYCLES PER BATCH UnOp END	CYCLES PER BATCH OFFSET (HRS)	CYCLES PER PROCESS UnOp START	CYCLES PER PROCESS UnOp END	CYCLES PER PROCESS OFFSET (HRS)	RECOVERY PRODUCT SWR	RECOVERY PRODUCT OAR	RECOVERY TOTAL PROTEIN SWR	RECOVERY TOTAL PROTEIN OAR
1	4	INITIAL SEEDING	1	1			1						
2	5	CULTURE VESSEL SPLIT	1	1			1						
3	5	CULTURE VESSEL SPLIT	1	1			1						
4	5	CULTURE VESSEL SPLIT	1	1			1						
5	6	SPINNER FLASK SPLIT	1	1			1						
6	54	SPINNER FLASK SPLIT	1	1			1						
7	13	STIRRED TANK REACTOR	1	1			1						
8	61	HARVEST/FEED	7	1			8	8	10 168				
9	62	HARVEST POOL	1	1			8	8	10 168				
10	34	MF/TANGENTIAL FLOW	1	1			8	8	10 168				
11	36	UF/CONCENTRATION	1	1			8	8	10 168				
12	39	PAC/HPLC	1	1			8	8	10 168				
13	39	PAC/HPLC	1	1			8	8	10 168				
14	36	UF/CONCENTRATION	1	1			8	8	10 168				
15	39	PAC/HPLC	1	1			8	8	10 168				
16	37	UF/FLOW DIALYSIS	1	1			8	8	10 168				
17	39	PAC/HPLC	1	1			8	8	10 168				
18	35	MF/DEAD END	1	1			8	8	10 168				
19	99	END	1	1			8	8	10 168				

402 404 406 408 410 412 414 416 418 420 422 424

FIG. 5

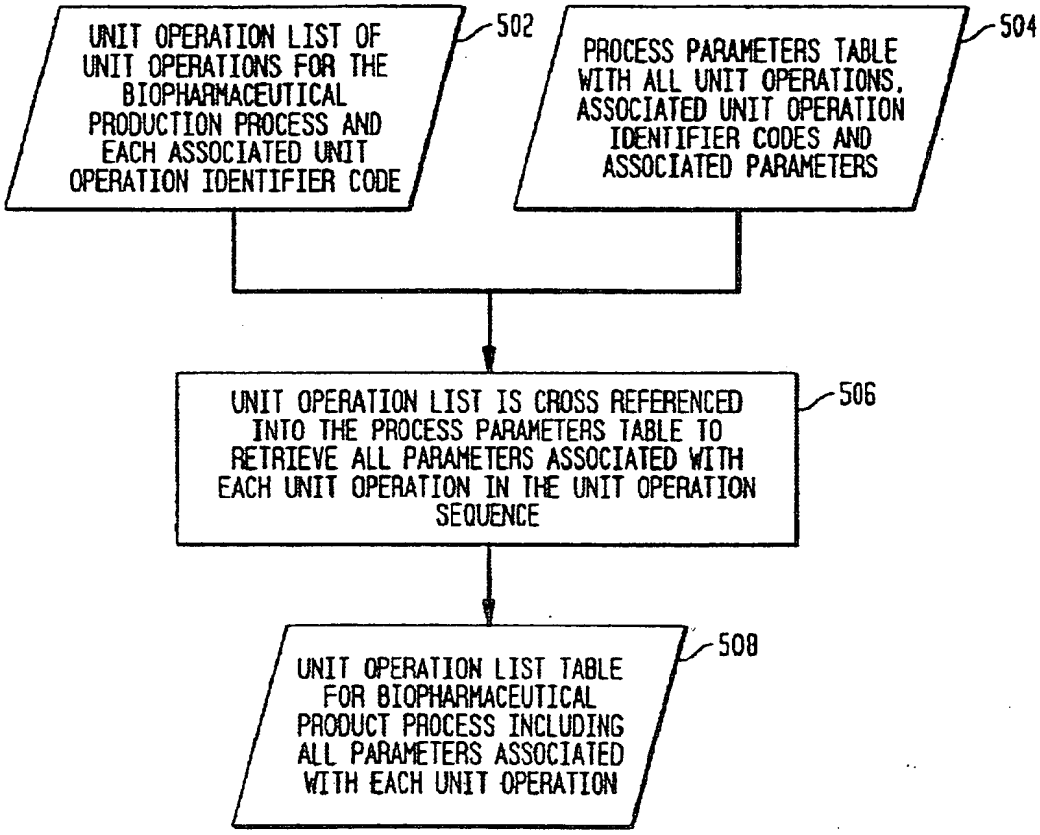

UNIT OPERATION LIST OF UNIT OPERATIONS FOR THE BIOPHARMACEUTICAL PRODUCTION PROCESS AND EACH ASSOCIATED UNIT OPERATION IDENTIFIER CODE
502
PROCESS PARAMETERS TABLE WITH ALL UNIT OPERATIONS, ASSOCIATED UNIT OPERATION IDENTIFIER CODES AND ASSOCIATED PARAMETERS
504
UNIT OPERATION LIST IS CROSS REFERENCED INTO THE PROCESS PARAMETERS TABLE TO RETRIEVE ALL PARAMETERS ASSOCIATED WITH EACH UNIT OPERATION IN THE UNIT OPERATION SEQUENCE
506
UNIT OPERATION LIST TABLE FOR BIOPHARMACEUTICAL PRODUCT PROCESS INCLUDING ALL PARAMETERS ASSOCIATED WITH EACH UNIT OPERATION
508

FIG. 6A

UNIT OPERATION ID CODE	UNIT OPERATION TYPE	PARAMETERS
1	INOCULUM PREP	# OF FLASKS, VOLUME OF FLASKS, TEMPERATURE, AGITATION, DURATION, FINAL OD
2	FLASK GROWTH	SCALE UP RATIO, MEDIA VOLUME, TEMPERATURE, AGITATION, DURATION, FINAL OD
3	FERMENTATION SEED	SCALE UP RATIO, FERMENTOR WORKING VOLUME, ANTIFOAM, BASE ACID, GROW TEMPERATURE, AGITATION, SPARGE RATE, BACK PRESSURE, TOTAL DURATION
4	FERMENTATION PRODUCTION	SCALE UP RATIO, GERMENTOR WORKING VOLUME, ANTIFOAM A, ANTIFOAM B, BASE, ACID, GROW TEMPERATURE, AGITATION, SPARGE RATE, BACK PRESSURE, TOTAL DURATION, FINAL OK, DRY CELL MASS, PRODUCT CONCENTRATION, CIP, SIP
5	HEAT EXCHANGE	PROCESS INITIAL & FINAL TEMP; UTILITY INITIAL & FINAL TEMP; PROCESS SPECIFIC HEAT; DESIGN TYPE, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
6	BATCH CENTRIFUGATION	SYSTEM VOID VOLUME, RCF, TIME, VOLUME REDUCTION, WASH VOLUME, CLEAN, RINSE
7	RESOLUBLIZATION RESUSPENSION	REAGENT/PRODUCT RATIO, TITRATION SOLUTION, RESOLUBLIZATION, AGITATION, SOLUTION NAME, STEP RECOVERY OF THE PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
8	CELL DISRUPTION HIGH PRESS. HOMOGENIZATION	PRODUCT TEMPPERATURE, UNILITY TEMPERATURE, VOID VOLUME, NUMBER OF PASSES, PRESSURE, FLOW RATE, TEMPERATURE INCREASE, WASH, RINSE, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPPERATURE REGULATION, CIP
9	DILUTE WITH SURFACTANT	REAGENT PRODUCT RATIO, TITRATION SOLUTION, DILUTION TIME, AGITATION, SOLUTION NAME, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
10	BATCH CENTRIFUGATION PRECIPITATE HARVEST	SYSTEM VOID VOLUME, RCF, TIME, VOLUME REDUCTION, WASH VOLUME, CLEAN, RINSE, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
11	RESUSPEND WITH CHAOTROPE	REAGENT/PRODUCT RATIO, TITRATION SOLUTION, RESOLUBLIZATION, AGITATION, SOLUTION NAME, STEP RECOVERY OF PRODUCT, STEP RECOVERY TO TP, TEMPERATURE REGULATION, CIP, SIP
.	.	.
.	.	.
.	.	.
.	.	.

FIG. 6B

504

SOLUTION TYPE	TASKS	TASK DURATION
S-101	SETUP, PREINCUBATION, INCUBATION, CLEAN UP	3, 3, 23, .3, HRS
S-101	SETUP, PREINCUBATION, INCUBATION, CLEAN UP	1, 1, 23, .3, HRS
S-101, 102, 103, 104, 105	SETUP, PREINCUBATION, FERMENTATION, HARVEST, CIP, SIP, CLEAN UP	1, 1, 21, .5, 1, 1, 3 HRS
S-101, 102 103, 104, 105	SETUP, PREINCUBATION, FERMENTATION, CIP, SIP, CLEAN UP	.
	SETUP, TRANSFER, CIP, SIP, CLEAN UP	.
S-106	SETUP, CENTRIFUGATION, WASH, CIP, SIP, CLEANUP	.
S-107	SETUP, DILUTION, AGITATE, CIP, SIP, CLEAN UP	.
S-107	SETUP, LYSIS, CIP, SIP, CLEAN UP	.
S-108	SETUP, DILUTION, AGITATE, CIP, SIP, CLEAN UP	.
S-108	SETUP, CENTRIFUGATION, WASH, CIP, SIP, CLEAN UP	.
S-109	SETUP, FLUSH, PRIME, CONCENTRATION, DILUTION, WASH, FLUSH, STORE, CIP, SIP, CLEANUP	.
.	.	.

. . .

FIG. 7

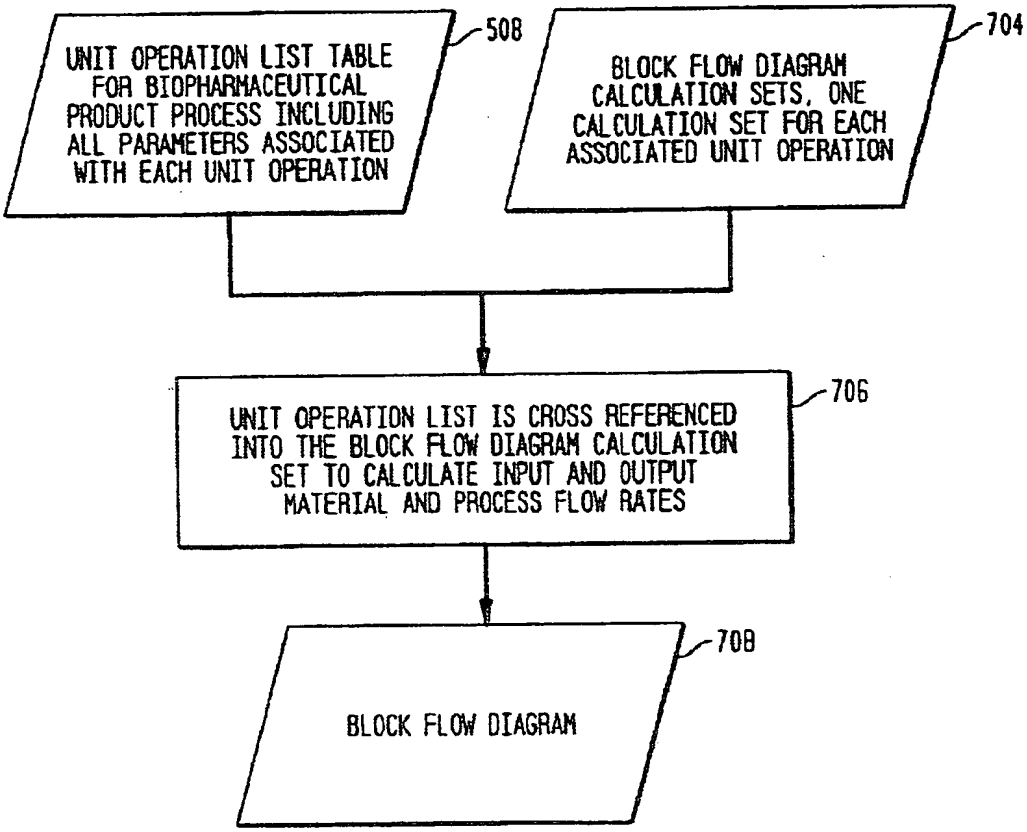

UNIT OPERATION LIST TABLE FOR BIOPHARMACEUTICAL PRODUCT PROCESS INCLUDING ALL PARAMETERS ASSOCIATED WITH EACH UNIT OPERATION
508
BLOCK FLOW DIAGRAM CALCULATION SETS, ONE CALCULATION SET FOR EACH ASSOCIATED UNIT OPERATION
704
UNIT OPERATION LIST IS CROSS REFERENCED INTO THE BLOCK FLOW DIAGRAM CALCULATION SET TO CALCULATE INPUT AND OUTPUT MATERIAL AND PROCESS FLOW RATES
706
BLOCK FLOW DIAGRAM
708

FIG. 8

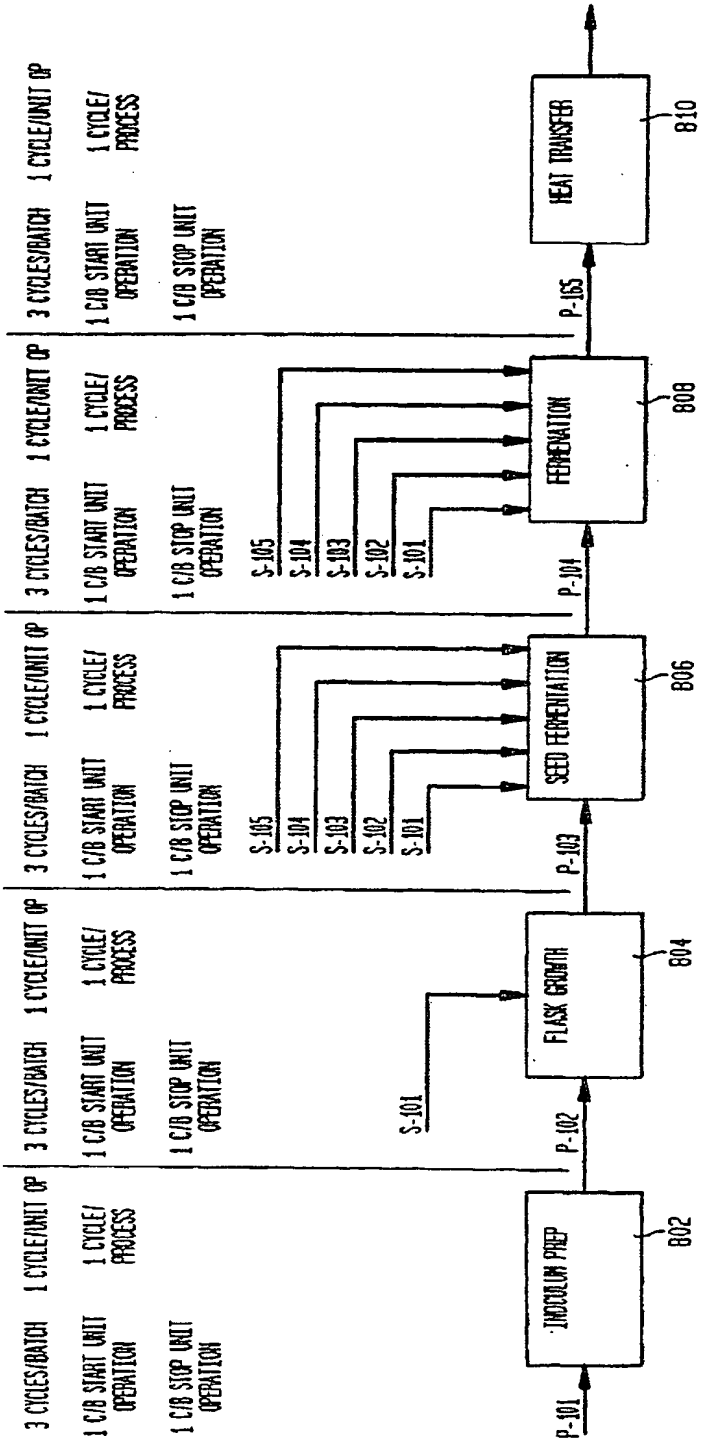

P-101
INOCULUM PREP
802
3 CYCLES/BATCH
1 C/B START UNIT OPERATION
1 C/B STOP UNIT OPERATION
1 CYCLE/UNIT OP
1 CYCLE/PROCESS
P-102
S-101
FLASK GROWTH
804
P-103
SEED FERMENTATION
806
S-101
S-102
S-103
S-104
S-105
P-104
FERMENTATION
808
P-105
HEAT TRANSFER
810

FIG. 9

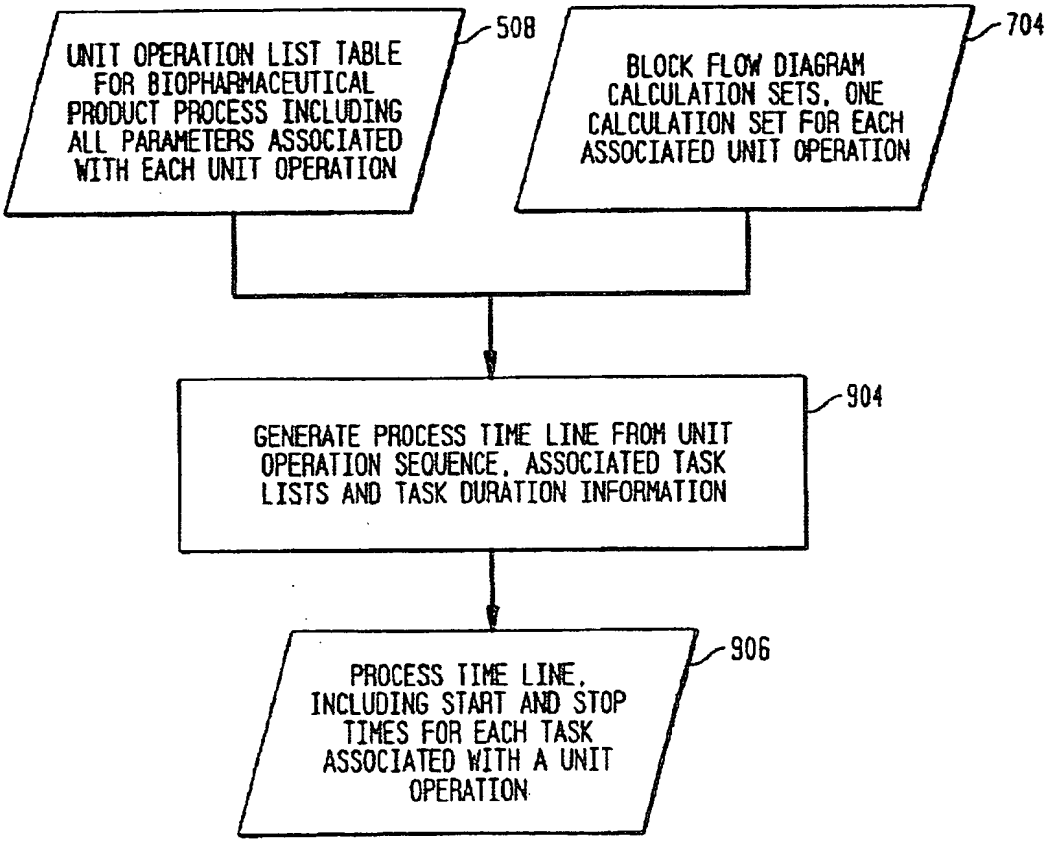

UNIT OPERATION LIST TABLE FOR BIOPHARMACEUTICAL PRODUCT PROCESS INCLUDING ALL PARAMETERS ASSOCIATED WITH EACH UNIT OPERATION
508
BLOCK FLOW DIAGRAM CALCULATION SETS, ONE CALCULATION SET FOR EACH ASSOCIATED UNIT OPERATION
704
GENERATE PROCESS TIME LINE FROM UNIT OPERATION SEQUENCE, ASSOCIATED TASK LISTS AND TASK DURATION INFORMATION
904
PROCESS TIME LINE, INCLUDING START AND STOP TIMES FOR EACH TASK ASSOCIATED WITH A UNIT OPERATION
906

FIG. 10

SAMPLE APPLICATION OF PROCESS DESIGN CYCLES IN PROCESS SCHEDULING

MICROBIAL FERMENTATION PROCESS (SEE UNIT OPERATION LIST)

			FIRST PROCESS CYCLE		SECOND PROCESS CYCLE	
		DURATION	WEEK	DAY	WEEK	DAY
NOTE: NONE OF THE UNIT OPERATIONS IN THIS PROCESS HAVE MORE THAT 1 CYCLE PER UNIT OPERATION						
(SEE UNIT OPERATION 8 IN THE MAMMALIAN CELL CULTURE PROCESS FOR AN EXAMPLE OF MULTIPLE CYCLES PER UNIT OPERATION)						
UNIT OPERATIONS 1-6 UNDERGO THREE REPETATIVE CYCLES PER BATCH AS A SET BEFORE CONTINUING WITH UNIT OP 7						
THIS TRANSLATES TO THREE RUNS ON A FERMENTOR WITH EACH HARVEST (UNIT OP 5 & 6) BEING STORED FOR POOLING AT UNIT OP 7						
ASSOCIATED WITH EACH FERMENTOR RUN (UNIT OP 4) ARE THE PREVIOUS STEPS FOR INNOCULATION PREP (UNIT OPS 1-3)						
1/3 FERMENTATION CYCLES PER BATCH						
1	INOCULUM PREP	24 HRS	1 FRI - SAT		2 FRI - SAT	
2	FLASK GROWTH	24 HRS	2 SAT - SUN		3 SAT - SUN	
3	SEED FERMENTAION	24 HRS	2 SUN - MON		3 SUN - MON	
4	PRODUCTION FERMENTATION	24 HRS	2 MON - TUE		3 MON - TUE	
5	HEAT EXCHANGE	1 HR	2 TUE		3 TUE	
6	CENTRIFUGATION	1 HR	2 TUE		3 TUE	
2/3 FERMENTATION CYCLES PER BATCH						
1	INOCULUM PREP	24 HRS	2 SUN - MON		3 SUN - MON	
2	FLASK GROWTH	24 HRS	2 MON - TUE		3 MON - TUE	
3	SEED FERMENTAION	24 HRS	2 TUE - WED		3 TUE - WED	
4	PRODUCTION FERMENTATION	24 HRS	2 WED - THU		3 WED - THU	
5	HEAT EXCHANGE	1 HR	2 THU		3 THU	
6	CENTRIFUGATION	1 HR	2 THU		3 THU	
3/3 FERMENTATION CYCLES PER BATCH						
1	INOCULUM PREP	24 HRS	2 TUE - WED		3 TUE - WED	
2	FLASK GROWTH	24 HRS	2 WED - THU		3 WED - THU	
3	SEED FERMENTAION	24 HRS	2 THU - FRI		3 THU - FRI	
4	PRODUCTION FERMENTATION	24 HRS	2 FRI - SAT		3 FRI - SAT	
5	HEAT EXCHANGE	1 HR	2 SAT		3 SAT	
6	CENTRIFUGATION	1 HR	2 SAT		3 SAT	
UNIT OPERATION 7 POOLS THE HARVESTS FROM THE THREE FERMENTATION CYCLES ABOVE						
7	POOL HARVESTS	3 HR	3 MON		4 MON	
UNIT OPERATIONS 8-9 UNDERGO THREE REPETATIVE CYCLES PER BATCH AS SET BEFORE CONTINUING WITH UNIT OPERATION 11						
THIS TRANSLATES TO THREE CONSECUTIVE PASSES THROUGH CELL DISRUPTOR (UNIT OP 9) WITH ITS ASSOCIATED HEAT EXCHANGERS						
(UNIT OP 8 & 10) AT THE INLET AND THE OUTLET OF THE CELL DISRUPTOR						
1/3 DISRUPTION CYCLES PER BATCH						
8	HEAT EXCHANGE					
9	CELL DISRUPTION					
10	HEAT EXCHANGE	0.5 HR	3 MON		4 MON	
2/3 DISRUPTION CYCLES PER BATCH						
8	HEAT EXCHANGE					
9	CELL DISRUPTION					
10	HEAT EXCHANGE	0.5 HR	3 MON		4 MON	
3/3 DISRUPTION CYCLES PER BATCH						
8	HEAT EXCHANGE					
9	CELL DISRUPTION					
10	HEAT EXCHANGE	0.5 HR	3 MON		4 MON	

FIG. 11

SAMPLE APPLICATION OF PROCESS DESIGN CYCLES IN PROCESS SCHEDULING

MICROBIAL FERMENTATION PROCESS (SEE UNIT OPERATION LIST)

			FIRST PROCESS CYCLE		SECOND PROCESS CYCLE	
		DURATION	WEEK	DAY	WEEK	DAY
UNIT OPS 11-12 UNDERGO TWO REPETATIVE CYCLES PER BATCH AS A SET BEFORE CONTINUING WITH UNIT OP 13 THIS TRANSLATES TO TWO CYCLES OF RESUSPENDING THE CELL LYSATE FROM THE CELL DISRUPTOR IN A MILD SURFACTANT AND RECONCENTRATING THE INSOLUBLE PRODUCT TO A PASTE BY CENTRIFUGATION						
1/2 PRODUCT WASHING CYCLES PER BATCH						
11	RESUSPENSION	0.5 HR	3 MON		4 MON	
12	CENTRIFUGATION	1 HR	3 MON		4 MON	
2/3 PRODUCT WASHING CYCLES PER BATCH						
11	RESUSPENSION	0.5 HR	3 MON		4 MON	
12	CENTRIFUGATION	1 HR	3 MON		4 MON	
UNIT OPS 13-22 UNDERGO ONLY ONE CYCLE PER UNIT OPERATION EACH TO THE END OF THE PROCESS						
13	RESUSPENSION	0.5 HR	3 MON		4 MON	
14	BUFFER EXCHANGE	2 HR	3 MON		4 MON	
15	FILTRATION	2 HR	3 MON		4 MON	
16	LIQUID CHROMATOGRAPHY	16 HRS	3 MON - TUE		4 MON - TUE	
17	LIQUID CHROMATOGRAPHY	4 HRS	3 TUE		4 TUE	
18	BUFFER EXCHANGE	2 HRS	3 TUE		4 TUE	
19	LIQUID CHROMATOGRAPHY	2 HRS	3 WED		4 WED	
20	BUFFER EXCHANGE	2 HRS	3 WED		4 WED	
21	LIQUID CHROMATOGRAPHY	2 HRS	3 WED		4 WED	
22	FILTRATION	2 HRS	3 WED		4 WED	

FIG. 12A-1

	OPERATION	PROCESS TIME LINE												CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS		START		FINISH		
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
1	1 A INOCULUM PREP													
2														
3	SET UP	3.0	0.0	3.0 HRS	12.5			0.40	0.52	06/03/96	09:30 AM	06/03/96	12:30 PM	
4	PREINCUBATION	3.0	0.0	3.0 HRS	15.5			0.52	0.65	06/03/96	12:30 PM	06/03/96	03:30 PM	
5	INCUBATION	23.0	0.0	23.0 HRS		38.5		0.65	1.60	06/03/96	03:30 PM	06/04/96	02:30 PM	
6	CLEAN UP	0.3	0.0	0.3 HRS			38.8	1.60	1.61	06/04/96	02:30 PM	06/04/96	02:45 PM	
6	SUBTOTAL	29.0		29.0 HRS		38.5								
7														
8	2 A FLASK GROWTH													
9														
10	SET UP	1.0	0.0	1.0 HRS	37.5			1.52	1.56	06/04/96	12:30 PM	06/04/96	01:30 PM	
11	PREINCUBATION	1.0	0.0	1.0 HRS	38.5			1.56	1.60	06/04/96	01:30 PM	06/04/96	02:30 PM	
12	INCUBATION	23.0	0.0	23.0 HRS		61.5		1.60	2.56	06/04/96	02:30 PM	06/05/96	01:30 PM	
13	CLEAN UP	0.3	0.0	0.3 HRS			61.8	2.56	2.57	06/05/96	01:30 PM	06/05/96	01:45 PM	
13	SUBTOTAL	25.0		25.0 HRS		61.5								
14														
15	3 A SEED FERMENTATION													
16														
17	SET UP	1.0	0.0	1.0 HRS	60.5			2.48	2.52	06/05/96	11:30 AM	06/05/96	12:30 PM	
18	PREINCUBATION	1.0	0.0	1.0 HRS	61.5			2.52	2.56	06/05/96	12:30 PM	06/05/96	01:30 PM	
19	FERMENTATION	21.0	0.0	21.0 HRS		82.5		2.56	3.44	06/05/96	01:30 PM	06/06/96	10:30 AM	
20	HARVEST	0.5	0.0	0.5 HRS		83.0		3.44	3.46	06/06/96	10:30 AM	06/06/96	11:00 AM	50.0 L 1.7 LPM = 0.50 HRS
21	CIP	1.0	0.0	1.0 HRS			83.5	3.44	3.48	06/06/96	10:30 AM	06/06/96	11:30 AM	
22	SIP	1.0	0.0	1.0 HRS			84.5	3.48	3.52	06/06/96	11:30 AM	06/06/96	12:30 PM	
23	CLEAN UP	3.0	0.0	3.0 HRS			87.5	3.52	3.65	06/06/96	12:30 PM	06/06/96	03:30 PM	
24	SUBTOTAL	28.5		28.5 HRS		83.0								
25														

FIG. 12A-2

| | | |

FIG. 12B-1

	OPERATION	PROCESS TIME LINE												CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS		START		FINISH		
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
59	INCUBATION	23.0	0.0	23.0 HRS		38.5		0.65	1.60	06/03/96	03:30 PM	06/04/96	02:30 PM	
60	CLEAN UP	0.3	0.0	0.3 HRS			38.8	1.60	1.61	06/04/96	02:30 PM	06/04/96	02:45 PM	
60	SUBTOTAL	25.0		25.0 HRS		38.5								
61														
62	2 B FLASK GROWTH													
63														
64	SET UP	1.0	0.0	1.0 HRS	37.5			1.52	1.56	06/04/96	12:30 PM	06/04/96	01:30 PM	
65	PREINCUBATION	1.0	0.0	1.0 HRS	38.5			1.56	1.60	06/04/96	01:30 PM	06/04/96	02:30 PM	
66	INCUBATION	23.0	0.0	23.0 HRS		61.5		1.60	2.56	06/04/96	02:30 PM	06/05/96	01:30 PM	
67	CLEAN UP	0.3	0.0	0.3 HRS			61.8	2.56	2.57	06/05/96	01:30 PM	06/05/96	01:45 PM	
67	SUBTOTAL	25.0		25.0 HRS		61.5								
68														
69	3 B SEED FERMENTATION													
70														
71	SET UP	1.0	0.0	1.0 HRS	60.5			2.48	2.52	06/05/96	11:30 AM	06/05/96	12:30 PM	
72	PREINCUBATION	1.0	0.0	1.0 HRS	61.5			2.52	2.56	06/05/96	12:30 PM	06/05/96	01:30 PM	
73	FERMENTATION	21.0	0.0	21.0 HRS		82.5		2.56	3.44	06/05/96	01:30 PM	06/06/96	10:30 AM	
74	HARVEST	0.5	0.0	0.5 HRS		83.0		3.44	3.46	06/06/96	10:30 AM	06/06/96	11:00 AM	50.0 L 1.7 LPH * 0.50 HRS
75	CIP	1.0	0.0	1.0 HRS			83.5	3.44	3.48	06/06/96	10:30 AM	06/06/96	11:30 AM	
76	SIP	1.0	0.0	1.0 HRS			84.5	3.48	3.52	06/06/96	11:30 AM	06/06/96	12:30 PM	
77	CLEAN UP	3.0	0.0	3.0 HRS			87.5	3.52	3.65	06/06/96	12:30 PM	06/06/96	03:30 PM	
78	SUBTOTAL	28.5		28.5 HRS		83.0								
79														
80	4 B PRODUCTION FERMENTATION													
81														
82	SET UP	1.0	0.0	1.0 HRS	82.0			3.38	3.42	06/06/96	09:00 AM	06/06/96	10:00 AM	
83	PREINCUBATION	1.0	0.0	1.0 HRS	83.0			3.42	3.46	06/06/96	10:00 AM	06/06/96	11:00 AM	
84	FERMENTATION	21.0	0.0	21.0 HRS		104.0		3.46	4.33	06/06/96	11:00 AM	06/07/96	08:00 AM	

FIG. 12B-2

| | | |

FIG. 12C-1

	OPERATION	PROCESS TIME LINE												CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS		START		FINISH		
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
116	2 C FLASK GROWTH													
117														
118	SET UP	1.0	0.0	1.0 HRS	37.5			1.52	1.56	06/04/96	12:30 PM	06/04/96	01:30 PM	
119	PREINCUBATION	1.0	0.0	1.0 HRS	38.5			1.56	1.60	06/04/96	01:30 PM	06/04/96	02:30 PM	
120	INCUBATION	23.0	0.0	23.0 HRS		61.5		1.60	2.56	06/04/96	02:30 PM	06/05/96	01:30 PM	
121	CLEAN UP	0.3	0.0	0.3 HRS			61.8	2.56	2.57	06/05/96	01:30 PM	06/05/96	01:45 PM	
121	SUBTOTAL	25.0		25.0 HRS		61.5								
122														
123	3 C SEED FERMENTATION													
124														
125	SET UP	1.0	0.0	1.0 HRS	60.5			2.48	2.52	06/05/96	11:30 AM	06/05/96	12:30 PM	
126	PREINCUBATION	1.0	0.0	1.0 HRS	61.5			2.52	2.56	06/05/96	12:30 PM	06/05/96	01:30 PM	
127	FERMENTATION	21.0	0.0	21.0 HRS		82.5		2.56	3.44	06/05/96	01:30 PM	06/06/96	10:30 AM	
128	HARVEST	0.5	0.0	0.5 HRS		83.0		3.44	3.46	06/06/96	10:30 AM	06/06/96	11:00 AM	50.0 L 1.7 LPM * 0.50 HRS
129	CIP	1.0	0.0	1.0 HRS			83.5	3.44	3.48	06/06/96	10:30 AM	06/06/96	11:30 AM	
130	SIP	1.0	0.0	1.0 HRS			84.5	3.48	3.52	06/06/96	11:30 AM	06/06/96	12:30 PM	
131	CLEAN UP	3.0	0.0	3.0 HRS			87.5	3.52	3.65	06/06/96	12:30 PM	06/06/96	03:30 PM	
132	SUBTOTAL	28.5		28.5 HRS		83.0								
133														
134	4 C PRODUCTION FERMENTATION													
135														
136	SET UP	1.0	0.0	1.0 HRS	82.0			3.38	3.42	06/06/96	09:00 AM	06/06/96	10:00 AM	
137	PREINCUBATION	1.0	0.0	1.0 HRS	83.0			3.42	3.46	06/06/96	10:00 AM	06/06/96	11:00 AM	
138	FERMENTATION	21.0	0.0	21.0 HRS		104.0		3.46	4.33	06/06/96	11:00 AM	06/07/96	08:00 AM	
139	CIP	1.0	0.0	1.0 HRS			105.0	4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM	
140	SIP	1.0	0.0	1.0 HRS			106.0	4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM	
141	CLEAN UP	2.0	0.0	2.0 HRS			108.0	4.42	4.50	06/07/96	10:00 AM	06/07/96	12:00 PM	
142	SUBTOTAL	27.0		27.0 HRS		104.0								

FIG. 12C-2

143																
144	5 C HEAT EXCHANGE															
145																
146	SET UP	0.50	0.0	0.5 HRS	104.5			4.33	4.35	06/07/96	08:00 AM	06/07/96	08:30 AM			
147	TRANSFER	1.00	0.0	1.0 HRS		105.0		4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM	562.1 LB	9.4 LPM	= 1.00 HRS
148	CIP	1.0	0.0	1.0 HRS			106.0	4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM			
149	SIP	1.0	0.0	1.0 HRS			107.0	4.42	4.46	06/07/96	10:00 AM	06/07/96	11:00 AM			
150	CLEAN UP	2.0	0.0	2.0 HRS			109.0	4.46	4.54	06/07/96	11:00 AM	06/07/96	01:00 PM			
151	SUBTOTAL	5.0		5.0 HRS		105.0										
152																
153	6 C CONT. CENT./SOLIDS															
154																
155	SET UP	1.00	0.0	1.0 HRS	105.0			4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM			
156	CENTRIFUGATION	1.00	0.0	1.0 HRS		106.0		4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM	562.1 LB	9.4 LPM	= 1.00 HRS
157	WASH	0.10	0.0	0.1 HRS		106.1		4.42	4.42	06/07/96	10:00 AM	06/07/96	10:06 AM	1.0 LB	0.2 LPM	= 0.10 HRS
158	CIP	0.25	0.0	0.3 HRS			106.4	4.42	4.43	06/07/96	10:06 AM	06/07/96	10:21 AM	20.0 LB	1.3 LPM	= 0.25 HRS
159	SIP	1.00	0.0	1.0 HRS			107.4	4.43	4.47	06/07/96	10:21 AM	06/07/96	11:21 AM			
160	CLEAN UP	0.50	0.0	0.5 HRS			107.9	4.47	4.49	06/07/96	11:21 AM	06/07/96	11:51 AM			
161	SUBTOTAL	3.85		3.85 HRS		106.1										
162																
163	7 A RESOLUBLIZATION															
164																
165	SET UP	1.00	0.0	1.0 HRS	106.1			4.38	4.42	06/07/96	09:06 AM	06/07/96	10:06 AM			
166	DILUTION	0.50	0.0	0.5 HRS		106.6		4.42	4.44	06/07/96	10:06 AM	06/07/96	10:36 AM	46.7 LB	1.6 LPM	= 0.50 HRS
167	AGITATE	1.00	0.0	1.0 HRS		107.6		4.44	4.48	06/07/96	10:36 AM	06/07/96	11:36 AM			0.50 HRS
168	CIP	1.00	0.0	1.0 HRS			108.6	4.48	4.53	06/07/96	11:36 AM	06/07/96	12:36 PM			
169	SIP	1.00	0.0	1.0 HRS			109.6	4.53	4.57	06/07/96	12:36 PM	06/07/96	01:36 PM			
170	CLEAN UP	1.00	0.0	1.0 HRS			110.6	4.57	4.61	06/07/96	01:36 PM	06/07/96	02:36 PM			
171	SUBTOTAL	5.50		5.50 HRS		107.6										
172																
173	8 A HEAT EXCHANGE															
174																

FIG. 12D-1

	OPERATION	PROCESS TIME LINE												CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS		START		FINISH		
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
175	SET UP	0.50	0.0	0.5 HRS	107.6			4.46	4.48	06/07/96	11:06 AM	06/07/96	11:36 AM	
176	TRANSFER	0.30	0.0	0.3 HRS		107.9		4.48	4.50	06/07/96	11:36 AM	06/07/96	11:54 AM	66.5 L@ 3.7 LPM = 0.30 HRS
177	CIP	0.0	0.0	0.0 HRS			107.9	4.50	4.50	06/07/96	11:54 AM	06/07/96	11:54 AM	
178	SIP	0.0	0.0	0.0 HRS			107.9	4.50	4.50	06/07/96	11:54 AM	06/07/96	11:54 AM	
179	CLEAN UP	0.0	0.0	0.0 HRS			107.9	4.50	4.50	06/07/96	11:54 AM	06/07/96	11:54 AM	
180	SUBTOTAL	0.8		0.8 HRS		107.9								
181														
182	9 A HOMOGENIZATION													
183														
184	SET UP	0.25	0.0	0.3 HRS	107.9			4.49	4.50	06/07/96	11:39 AM	06/07/96	11:54 AM	
185	LYSIS	0.68	0.0	0.7 HRS		108.6		4.50	4.52	06/07/96	11:54 AM	06/07/96	12:34 PM	66.5 L@ 1.6 LPM = 0.68 HRS
186	CIP	0.0	0.0	0.0 HRS			108.6	4.52	4.52	06/07/96	12:34 PM	06/07/96	12:34 PM	
187	SIP	0.0	0.0	0.0 HRS			108.6	4.52	4.52	06/07/96	12:34 PM	06/07/96	12:34 PM	
188	CLEAN UP	0.0	0.0	0.0 HRS			108.6	4.52	4.52	06/07/96	12:34 PM	06/07/96	12:34 PM	
189	SUBTOTAL	0.9		0.9 HRS		108.6								
190														
191	10 A HEAT EXCHANGE													
192														
193	SET UP	0.50	0.0	0.5 HRS	108.6			4.50	4.52	06/07/96	12:04 PM	06/07/96	12:34 PM	
194	TRANSFER	0.30	0.0	0.3 HRS		108.9		4.52	4.54	06/07/96	12:34 PM	06/07/96	12:52 PM	69.0 L@ 3.8 LPM = 0.30 HRS
195	CIP	0.0	0.0	0.0 HRS			108.9	4.54	4.54	06/07/96	12:52 PM	06/07/96	12:52 PM	
196	SIP	0.0	0.0	0.0 HRS			108.9	4.54	4.54	06/07/96	12:52 PM	06/07/96	12:52 PM	
197	CLEAN UP	0.0	0.0	0.0 HRS			108.9	4.54	4.54	06/07/96	12:52 PM	06/07/96	12:52 PM	
198	SUBTOTAL	0.8		0.8 HRS		108.9								
199														
200	8 B HEAT EXCHANGE													
201														
202	SET UP	0.00	0.0	0.0 HRS	108.9			4.54	4.54	06/07/96	12:52 PM	06/07/96	12:52 PM	

FIG. 12D-2

| | | |

FIG. 12E-1

	OPERATION	PROCESS TIME LINE				ABS. DAYS		START		FINISH		CALCULATIONS
		DURATION (HRS.)		REL. TIME SCALE (HRS)								
		CALC.	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
					15.5				06/03/96	08:00 AM			
235													
236	9 C HOMOGENIZATION												
237													
238	SET UP	0.00	0.0 HRS	110.5			4.60	4.60	06/07/96	02:27 PM	06/07/96	02:27 PM	
239	LYSIS	0.68	0.0 HRS		111.1		4.60	4.63	06/07/96	02:27 PM	06/07/96	03:07 PM	66.5 LB 1.6 LPM = 0.68 HRS
240	CIP	1.0	1.0 HRS			112.1	4.63	4.67	06/07/96	03:07 PM	06/07/96	04:07 PM	
241	SIP	1.0	1.0 HRS			113.1	4.67	4.71	06/07/96	04:07 PM	06/07/96	05:07 PM	
242	CLEAN UP	1.0	1.0 HRS			114.1	4.71	4.76	06/07/96	05:07 PM	06/07/96	06:07 PM	
243	SUBTOTAL	3.7	3.7 HRS		111.1								
244													
245	10 C HEAT EXCHANGE												
246													
247	SET UP	0.00	0.0 HRS	111.1			4.63	4.63	06/07/96	03:07 PM	06/07/96	03:07 PM	
248	TRANSFER	0.30	0.3 HRS		111.4		4.63	4.64	06/07/96	03:07 PM	06/07/96	03:23 PM	69.0 LB 3.8 LPM = 0.30 HRS
249	CIP	1.0	1.0 HRS			112.4	4.64	4.68	06/07/96	03:25 PM	06/07/96	04:25 PM	
250	SIP	1.0	1.0 HRS			113.4	4.68	4.73	06/07/96	04:25 PM	06/07/96	05:25 PM	
251	CLEAN UP	1.0	1.0 HRS			114.4	4.73	4.77	06/07/96	05:25 PM	06/07/96	06:25 PM	
252	SUBTOTAL	3.3	3.3 HRS		111.4								
253													
254	11 A RESOLUBILIZATION												
255													
256	SET UP	1.0	1.0 HRS	108.9			4.49	4.54	06/07/96	11:52 AM	06/07/96	12:52 PM	
257	DILUTION	0.5	0.5 HRS		109.4		4.54	4.56	06/07/96	12:52 PM	06/07/96	01:22 PM	206.9 LB 6.9 LPM = 0.50 HRS
258	AGITATE	0.5	0.5 HRS		109.9		4.56	4.58	06/07/96	01:22 PM	06/07/96	01:52 PM	0.50 HRS
259	CIP	0.0	0.0 HRS			109.9	4.58	4.58	06/07/96	01:52 PM	06/07/96	01:52 PM	
260	SIP	0.0	0.0 HRS			109.9	4.58	4.58	06/07/96	01:52 PM	06/07/96	01:52 PM	
261	CLEAN UP	0.0	0.0 HRS			109.9	4.58	4.58	06/07/96	01:52 PM	06/07/96	01:52 PM	
262	SUBTOTAL	2.0	2.0 HRS		109.9								

FIG. 12E-2

263																	
264	12 A CONT. CENT/SOLIDS																
265																	
266	SET UP	1.0	0.0	1.0 HRS	109.9			4.54	4.58	06/07/96	12:52 PM	06/07/96	01:52 PM				
267	CENTRIFUGATION	0.5	0.0	0.5 HRS		110.4		4.58	4.60	06/07/96	01:52 PM	06/07/96	02:22 PM	275.9 LB	9.2 LPM	=	0.50 HRS
268	WASH	0.1	0.0	0.1 HRS		110.5		4.60	4.60	06/07/96	02:22 PM	06/07/96	02:28 PM	3.0 LB	0.5 LPM	=	0.10 HRS
269	CIP	0.0	0.0	0.0 HRS			110.5	4.60	4.60	06/07/96	02:28 PM	06/07/96	02:28 PM	8.0 LB	0.5 LPM	=	0.25 HRS
270	SIP	0.0	0.0	0.0 HRS			110.5	4.60	4.60	06/07/96	02:28 PM	06/07/96	02:28 PM				
271	CLEAN UP	0.0	0.0	0.0 HRS			110.5	4.60	4.60	06/07/96	02:28 PM	06/07/96	02:28 PM				
272	SUBTOTAL	1.6		1.6 HRS		110.5											
273																	
274	11 B RESOLUBLIZATION																
275																	
276	SET UP	0.0	0.0	0.0 HRS	110.5			4.60	4.60	06/07/96	02:28 PM	06/07/96	02:28 PM				
277	DILUTION	0.5	0.0	0.5 HRS		111.0		4.60	4.62	06/07/96	02:28 PM	06/07/96	02:58 PM	206.9 LB	6.9 LPM	=	0.50 HRS
278	AGITATE	0.3	0.0	0.3 HRS		111.2		4.62	4.63	06/07/96	02:58 PM	06/07/96	03:13 PM				0.50 HRS
279	CIP	1.0	0.0	1.0 HRS			112.2	4.63	4.68	06/07/96	03:13 PM	06/07/96	04:13 PM				
280	SIP	1.0	0.0	1.0 HRS			113.2	4.68	4.72	06/07/96	04:13 PM	06/07/96	05:13 PM				
281	CLEAN UP	1.0	0.0	1.0 HRS			114.2	4.72	4.76	06/07/96	05:13 PM	06/07/96	06:13 PM				
282	SUBTOTAL	3.8		3.8 HRS		111.2											
283																	
284	12 B CONT. CENT/SOLIDS																
285																	
286	SET UP	1.0	0.0	1.0 HRS	111.2			4.59	4.63	06/07/96	02:13 PM	06/07/96	03:13 PM				
287	CENTRIFUGATION	0.5	0.0	0.5 HRS		111.7		4.63	4.66	06/07/96	03:13 PM	06/07/96	03:43 PM	275.9 LB	9.2 LPM	=	0.50 HRS
288	WASH	0.1	0.0	0.1 HRS		111.8		4.66	4.66	06/07/96	03:43 PM	06/07/96	03:49 PM	3.0 LB	0.5 LPM	=	0.10 HRS
289	CIP	0.3	0.0	0.3 HRS			112.1	4.66	4.67	06/07/96	03:49 PM	06/07/96	04:04 PM	8.0 LB	0.5 LPM	=	0.25 HRS
290	SIP	1.0	0.0	1.0 HRS			113.1	4.67	4.71	06/07/96	04:04 PM	06/07/96	05:04 PM				
291	CLEAN UP	0.5	0.0	0.5 HRS			113.6	4.71	4.73	06/07/96	05:04 PM	06/07/96	05:34 PM				
292	SUBTOTAL	3.4		3.4 HRS		111.8											
293																	
294	13 A RESOLUBLIZATION																

FIG. 12F-1

	OPERATION	PROCESS TIME LINE								START		FINISH		CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS						
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
295														
296	SET UP	1.0	0.0	1.0 HRS	110.5			4.56	4.60	06/07/96	01:28 PM	06/07/96	02:28 PM	
297	DILUTION	0.5	0.0	0.5 HRS		111.0		4.60	4.62	06/07/96	02:28 PM	06/07/96	02:58 PM	60.7 L@ 2.0 LPM = 0.50 HRS
298	AGITATE	18.0	0.0	18.0 HRS		129.0		4.62	5.37	06/07/96	02:58 PM	06/08/96	08:58 AM	23.50 HRS
299	CIP	1.0	0.0	1.0 HRS			130.0	5.37	5.42	06/08/96	08:58 AM	06/08/96	09:58 AM	
300	SIP	1.0	0.0	1.0 HRS			131.0	5.42	5.46	06/08/96	09:58 AM	06/08/96	10:58 AM	
301	CLEAN UP	1.0	0.0	1.0 HRS			132.0	5.46	5.50	06/08/96	10:58 AM	06/08/96	11:58 AM	
302	SUBTOTAL	22.5		22.5 HRS		129.0								
303														
304	14 A CONCENTRATION													26.99 SF
305														
306	SET UP	1.0	0.0	1.0 HRS	127.6			5.28	5.32	06/08/96	06:38 AM	06/08/96	07:38 AM	
307	FLUSH	0.7	0.0	0.7 HRS	128.3			5.32	5.35	06/08/96	07:38 AM	06/08/96	08:18 AM	54.0 L@ 3.0 L/SF/Hr or 1.35 LPM
308	PRIME	0.7	0.0	0.7 HRS	129.0			5.35	5.37	06/08/96	08:18 AM	06/08/96	08:58 AM	54.0 L@ 3.0 L/SF/Hr or 1.35 LPM
309	CONCENTRATION	1.0	0.0	1.0 HRS		130.0		5.37	5.42	06/08/96	08:58 AM	06/08/96	09:58 AM	81.0 L@ 3.0 L/SF/Hr or 1.35 LPM
310	DILUTION	0.4	0.0	0.4 HRS		130.4		5.42	5.43	06/08/96	09:58 AM	06/08/96	10:25 AM	13.5 L@ 0.5 LPM
311	WASH	0.9	0.0	0.9 HRS		131.3		5.43	5.47	06/08/96	10:25 AM	06/08/96	11:19 AM	72.9 L@ 3.0 L/SF/Hr or 1.35 LPM
312	FLUSH	0.3	0.0	0.3 HRS			131.7	5.47	5.49	06/08/96	11:19 AM	06/08/96	11:39 AM	27.0 L@ 3.0 L/SF/Hr or 1.35 LPM
313	STORE	0.7	0.0	0.7 HRS			132.3	5.49	5.51	06/08/96	11:39 AM	06/08/96	12:19 PM	54.0 L@ 3.0 L/SF/Hr or 1.35 LPM
314	CIP	1.0	0.0	1.0 HRS			133.3	5.51	5.56	06/08/96	12:19 PM	06/08/96	01:19 PM	
315	SIP	1.0	0.0	1.0 HRS			134.3	5.56	5.60	06/08/96	01:19 PM	06/08/96	02:19 PM	
316	CLEAN UP	1.0	0.0	1.0 HRS			135.3	5.60	5.64	06/08/96	02:19 PM	06/08/96	03:19 PM	
317	SUBTOTAL	8.7		8.7 HRS		131.3								MAX FR 1.35 LPM
318														
319	15 A MICROFILTRATION													12.60 SF
320														
321	SET UP	1.0	0.0	1.0 HRS	131.1			5.42	5.46	06/08/96	10:03 AM	06/08/96	11:03 AM	
322	FLUSH	0.1	0.0	0.1 HRS	131.2			5.46	5.47	06/08/96	11:03 AM	06/08/96	11:11 AM	25.2 L@ 15.0 L/SF/Hr or 3.15 LPM
323	PRIME	0.1	0.0	0.1 HRS	131.3			5.47	5.47	06/08/96	11:11 AM	06/08/96	11:19 AM	25.2 L@ 15.0 L/SF/Hr or 3.15 LPM

FIG. 12F-2

324	FILTRATION	0.5	0.0	0.5 HRS		131.8		5.47	5.49	06/08/96	11:19 AM	06/08/96	11:49 AM	94.5 LB	15.0 L/SF/Hr or 3.15 LPM
325	WASH	0.0	0.0	0.0 HRS		131.8		5.49	5.49	06/08/96	11:49 AM	06/08/96	11:49 AM	0.0 LB	15.0 L/SF/Hr or 3.15 LPM
326	REGENERATE	0.0	0.0	0.0 HRS			131.9	5.49	5.49	06/08/96	11:49 AM	06/08/96	11:51 AM	6.3 LB	15.0 L/SF/Hr or 3.15 LPM
327	STORE	0.1	0.0	0.1 HRS			131.9	5.49	5.50	06/08/96	11:51 AM	06/08/96	11:55 AM	12.6 LB	15.0 L/SF/Hr or 3.15 LPM
328	CIP	1.0	0.0	1.0 HRS			132.9	5.50	5.54	06/08/96	11:55 AM	06/08/96	12:55 PM		
329	SIP	1.0	0.0	1.0 HRS			133.9	5.54	5.58	06/08/96	12:55 PM	06/08/96	01:55 PM		
330	CLEAN UP	1.0	0.0	1.0 HRS			134.9	5.58	5.62	06/08/96	01:55 PM	06/08/96	02:55 PM		
331	SUBTOTAL	4.9		4.9 HRS		131.8									
332															
333	16 A P/A HPLC													63.8 L.CV	0.4 H/D 60.32 CM DIA.
334															
335	EQUILIBRATION	1.1	0.0	1.1 HRS	131.4			5.43	5.48	06/08/96	10:17 AM	06/08/96	11:24 AM	318.9 LB	100.0 CM/HR or 4.76 LPM
336	LOAD	0.7	0.0	0.7 HRS		132.5		5.49	5.52	06/08/96	11:49 AM	06/08/96	12:31 PM	100.5 LB	50.0 CM/HR or 2.38 LPM
337	WASH	1.3	0.0	1.3 HRS		133.9		5.52	5.58	06/08/96	12:31 PM	06/08/96	01:52 PM	191.4 LB	50.0 CM/HR or 2.38 LPM
338	ELUTE A	1.3	0.0	1.3 HRS		135.2		5.58	5.63	06/08/96	01:52 PM	06/08/96	03:12 PM	191.4 LB	50.0 CM/HR or 2.38 LPM
339	ELUTE B	0.0	0.0	0.0 HRS		135.2		5.63	5.63	06/08/96	03:12 PM	06/08/96	03:12 PM	0.0 LB	30.0 CM/HR or 1.43 LPM
340	REGENERATE	0.2	0.0	0.2 HRS			135.4	5.63	5.64	06/08/96	03:12 PM	06/08/96	03:25 PM	63.8 LB	100.0 CM/HR or 4.76 LPM
341	STORE	0.4	0.0	0.4 HRS			135.9	5.64	5.66	06/08/96	03:25 PM	06/08/96	03:52 PM	127.6 LB	100.0 CM/HR or 4.76 LPM
342	CIP	1.0	0.0	1.0 HRS			136.9	5.66	5.70	06/08/96	03:52 PM	06/08/96	04:52 PM		
343	SIP	1.0	0.0	1.0 HRS			137.9	5.70	5.74	06/08/96	04:52 PM	06/08/96	05:52 PM		
344	CLEAN UP	1.0	0.0	1.0 HRS			138.9	5.74	5.79	06/08/96	05:52 PM	06/08/96	06:52 PM		
345	SUBTOTAL	5.2		5.2 HRS		135.2								MAX FR	4.76 LPM
346															
347															
348	17 A P/A HPLC													12.2 L.CV	0.4 H/D 34.75 CM DIA.
349															
350	EQUILIBRATION	0.6	0.0	0.6 HRS	135.6			5.62	5.65	06/08/96	02:59 PM	06/08/96	03:38 PM	61.0 LB	100.0 CM/HR or 1.58 LPM
351	LOAD	1.1	0.0	1.1 HRS		136.3		5.63	5.68	06/08/96	03:12 PM	06/08/96	04:17 PM	51.0 LB	50.0 CM/HR or 0.79 LPM
352	WASH	0.8	0.0	0.8 HRS		137.1		5.68	5.71	06/08/96	04:17 PM	06/08/96	05:03 PM	36.6 LB	50.0 CM/HR or 0.79 LPM
353	ELUTE A	0.8	0.0	0.8 HRS		137.8		5.71	5.74	06/08/96	05:03 PM	06/08/96	05:49 PM	36.6 LB	50.0 CM/HR or 0.79 LPM
354	ELUTE B	0.0	0.0	0.0 HRS		137.8		5.74	5.74	06/08/96	05:49 PM	06/08/96	05:49 PM	0.0 LB	30.0 CM/HR or 0.47 LPM

FIG. 12G-1

	OPERATION	PROCESS TIME LINE								START		FINISH		CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS						
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
355	REGENERATE	0.1	0.0	0.1 HRS			138.0	5.74	5.75	06/08/96	05:49 PM	06/08/96	05:57 PM	12.2 LB 100.0 CM/HR or 1.58 LPM
356	STORE	0.3	0.0	0.3 HRS			138.2	5.75	5.76	06/08/96	05:57 PM	06/08/96	06:13 PM	24.4 LB 100.0 CM/HR or 1.58 LPM
357	CIP	1.0	0.0	1.0 HRS			139.2	5.76	5.80	06/08/96	06:13 PM	06/08/96	07:13 PM	
358	SIP	1.0	0.0	1.0 HRS			140.2	5.80	5.84	06/08/96	07:13 PM	06/08/96	08:13 PM	
359	CLEAN UP	1.0	0.0	1.0 HRS			141.2	5.84	5.88	06/08/96	08:13 PM	06/08/96	09:13 PM	
360	SUBTOTAL	6.7		6.7 HRS		137.8								
361														MAX FR 1.58 LPM
362	1B A FLOW DIALYSIS													
363														12.20 SF
364	SET UP	1.0	0.0	1.0 HRS	136.5			5.65	5.69	06/08/96	03:29 PM	06/08/96	04:29 PM	
365	FLUSH	0.7	0.0	0.7 HRS	137.2			5.69	5.72	06/08/96	04:29 PM	06/08/96	05:09 PM	24.4 LB 3.0 L/SF/Hr or 0.61 LPM
366	PRIME	0.7	0.0	0.7 HRS	137.8			5.72	5.74	06/08/96	05:09 PM	06/08/96	05:49 PM	24.4 LB 3.0 L/SF/Hr or 0.61 LPM
367	DIALYSIS	1.0	0.0	1.0 HRS		138.8		5.74	5.78	06/08/96	05:49 PM	06/08/96	06:49 PM	36.6 LB 3.0 L/SF/Hr or 0.61 LPM
368	WASH	0.0	0.0	0.0 HRS		138.8		5.78	5.78	06/08/96	06:49 PM	06/08/96	06:49 PM	0.0 LB 3.0 L/SF/Hr or 0.61 LPM
369	FLUSH	0.3	0.0	0.3 HRS			139.2	5.78	5.80	06/08/96	06:49 PM	06/08/96	07:09 PM	12.2 LB 3.0 L/SF/Hr or 0.61 LPM
370	STORE	0.7	0.0	0.7 HRS			139.8	5.80	5.83	06/08/96	07:09 PM	06/08/96	07:49 PM	24.4 LB 3.0 L/SF/Hr or 0.61 LPM
371	CIP	1.0	0.0	1.0 HRS			140.8	5.83	5.87	06/08/96	07:49 PM	06/08/96	08:49 PM	
372	SIP	1.0	0.0	1.0 HRS			141.8	5.87	5.91	06/08/96	08:49 PM	06/08/96	09:49 PM	
373	CLEAN UP	1.0	0.0	1.0 HRS			142.8	5.91	5.95	06/08/96	09:49 PM	06/08/96	10:49 PM	
374	SUBTOTAL	7.3		7.3 HRS		138.8								
375														MAX FR 0.61 LPM
376	1B A P/A HPLC													
377														7.0 L.CV 0.4 H/D 28.81 CM DIA.
378	EQUILIBRATION	0.5	0.0	0.5 HRS	138.5			5.75	5.77	06/08/96	05:59 PM	06/08/96	06:31 PM	34.8 LB 100.0 CM/HR or 1.09 LPM
379	LOAD	0.2	0.0	0.2 HRS		139.1		5.78	5.79	06/08/96	06:49 PM	06/08/96	07:03 PM	7.3 LB 50.0 CM/HR or 0.54 LPM
380	WASH	0.6	0.0	0.6 HRS		139.7		5.79	5.82	06/08/96	07:03 PM	06/08/96	07:41 PM	20.9 LB 50.0 CM/HR or 0.54 LPM
381	ELUTE A	0.6	0.0	0.6 HRS		140.3		5.82	5.85	06/08/96	07:41 PM	06/08/96	08:20 PM	20.9 LB 50.0 CM/HR or 0.54 LPM
382	ELUTE B	0.0	0.0	0.0 HRS		140.3		5.85	5.85	06/08/96	08:20 PM	06/08/96	08:20 PM	0.0 LB 30.0 CM/HR or 0.33 LPM
383	REGENERATE	0.1	0.0	0.1 HRS			140.4	5.85	5.85	06/08/96	08:20 PM	06/08/96	08:26 PM	7.0 LB 100.0 CM/HR or 1.09 LPM

FIG. 12G-2

384	STORE	0.2	0.0	0.2 HRS			140.7	5.85	5.86	06/08/96	08:26 PM	06/08/96	08:39 PM	13.9 LB 100.0 CM/HR or 1.09 LPM
385	CIP	1.0	0.0	1.0 HRS			141.7	5.86	5.90	06/08/96	08:39 PM	06/08/96	09:39 PM	
386	SIP	1.0	0.0	1.0 HRS			142.7	5.90	5.94	06/08/96	09:39 PM	06/08/96	10:39 PM	
387	CLEAN UP	1.0	0.0	1.0 HRS			143.7	5.94	5.99	06/08/96	10:39 PM	06/08/96	11:39 PM	
388	SUBTOTAL	5.4		5.4 HRS		140.3								
389														MAX FR 1.09 LPM
390	20 A FLOW DIALYSIS													
391														2.43 SF
392	SET UP	0.0	0.0	0.0 HRS	139.0			5.79	5.79	06/08/96	07:00 PM	06/08/96	07:00 PM	
393	FLUSH	0.7	0.0	0.7 HRS	139.7			5.79	5.82	06/08/96	07:00 PM	06/08/96	07:40 PM	4.9 LB 3.0 L/SF/HR or 0.12 LPM
394	PRIME	0.7	0.0	0.7 HRS	140.3			5.82	5.85	06/08/96	07:40 PM	06/08/96	08:20 PM	4.9 LB 3.0 L/SF/HR or 0.12 LPM
395	DIALYSIS	2.0	0.0	2.0 HRS		142.3		5.85	5.93	06/08/96	08:20 PM	06/08/96	10:20 PM	14.6 LB 3.0 L/SF/HR or 0.12 LPM
396	WASH	0.0	0.0	0.0 HRS		142.3		5.93	5.93	06/08/96	10:20 PM	06/08/96	10:20 PM	0.0 LB 3.0 L/SF/HR or 0.12 LPM
397	FLUSH	0.3	0.0	0.3 HRS			142.7	5.93	5.94	06/08/96	10:20 PM	06/08/96	10:40 PM	2.4 LB 3.0 L/SF/HR or 0.12 LPM
398	STORE	0.7	0.0	0.7 HRS			143.3	5.94	5.97	06/08/96	10:40 PM	06/08/96	11:20 PM	4.9 LB 3.0 L/SF/HR or 0.12 LPM
399	CIP	0.0	0.0	0.0 HRS			143.3	5.97	5.97	06/08/96	11:20 PM	06/08/96	11:20 PM	
400	SIP	0.0	0.0	0.0 HRS			143.3	5.97	5.97	06/08/96	11:20 PM	06/08/96	11:20 PM	
401	CLEAN UP	0.0	1.0	1.0 HRS			144.3	5.97	6.01	06/08/96	11:20 PM	06/08/96	12:20 AM	
402	SUBTOTAL	4.3		5.3 HRS		142.3								
403														MAX FR 0.12 LPM
404	17 A P/A HPLC													
405														5.3 L.CY 0.4 H/D 26.35 CM DIA.
406	EQUILIBRATION	0.5	0.0	0.5 HRS	142.0			5.89	5.91	06/08/96	09:28 PM	06/08/96	09:57 PM	26.6 LB 100.0 CM/HR or 0.91 LPM
407	LOAD	0.1	0.0	0.1 HRS		142.4		5.93	5.94	06/08/96	10:20 PM	06/08/96	10:26 PM	2.9 LB 50.0 CM/HR or 0.45 LPM
408	WASH	0.6	0.0	0.6 HRS		143.0		5.94	5.96	06/08/96	10:26 PM	06/08/96	11:01 PM	16.0 LB 50.0 CM/HR or 0.45 LPM
409	ELUTE A	0.6	0.0	0.6 HRS		143.6		5.96	5.96	06/08/96	11:01 PM	06/08/96	11:36 PM	16.0 LB 50.0 CM/HR or 0.45 LPM
410	ELUTE B	0.0	0.0	0.0 HRS		143.6		5.96	5.98	06/08/96	11:36 PM	06/08/96	11:36 PM	0.0 LB 30.0 CM/HR or 0.27 LPM
411	REGENERATE	0.1	0.0	0.1 HRS			143.7	5.98	5.99	06/08/96	11:36 PM	06/08/96	11:42 PM	5.3 LB 100.0 CM/HR or 0.91 LPM
412	STORE	0.2	0.0	0.2 HRS			143.9	5.99	6.00	06/08/96	11:42 PM	06/08/96	11:54 PM	10.6 LB 100.0 CM/HR or 0.91 LPM
413	CIP	0.0	0.0	0.0 HRS			143.9	6.00	6.00	06/08/96	11:54 PM	06/08/96	11:54 PM	
414	SIP	0.0	0.0	0.0 HRS			143.9	6.00	6.00	06/08/96	11:54 PM	06/08/96	11:54 PM	

FIG. 12H

	OPERATION	PROCESS TIME LINE												CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS		START		FINISH		
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
415	CLEAN UP	1.0	0.0	1.0 HRS			141.9	6.00	6.04	06/08/96	11:54 PM	06/09/96	12:54 AM	
416	SUBTOTAL	2.1		2.1 HRS		143.6								MAX FR 0.91 LPM
417														
418	22 A STERILE FILTRATION													0.09 SF
419														
420	SET UP	0.5	0.0	0.5 HRS	152.6			6.34	6.36	06/03/96	08:06 AM	06/09/96	06:36 AM	
421	FILTRATION	0.5	0.0	0.5 HRS		144.1		5.98	6.00	06/08/96	11:36 PM	06/09/96	12:06 AM	2.2 LB 50.0 L/SF/Hr or 0.07 LPM
422	STORAGE	0.5	0.0	0.5 HRS			144.6	6.00	6.03	06/09/96	12:06 AM	06/09/96	12:36 AM	
423	CIP	0.0	0.0	0.0 HRS			144.6	6.03	6.03	06/09/96	12:36 AM	06/09/96	12:36 AM	
424	SIP	0.0	0.0	0.0 HRS			144.6	6.03	6.03	06/09/96	12:36 AM	06/09/96	12:36 AM	
425	CLEAN UP	1.0	0.0	1.0 HRS			145.6	6.03	6.07	06/09/96	12:36 AM	06/09/96	01:36 AM	
426	SUBTOTAL	1.5		1.5 HRS		144.1								MAX FR 0.07 LPM

FIG. 13

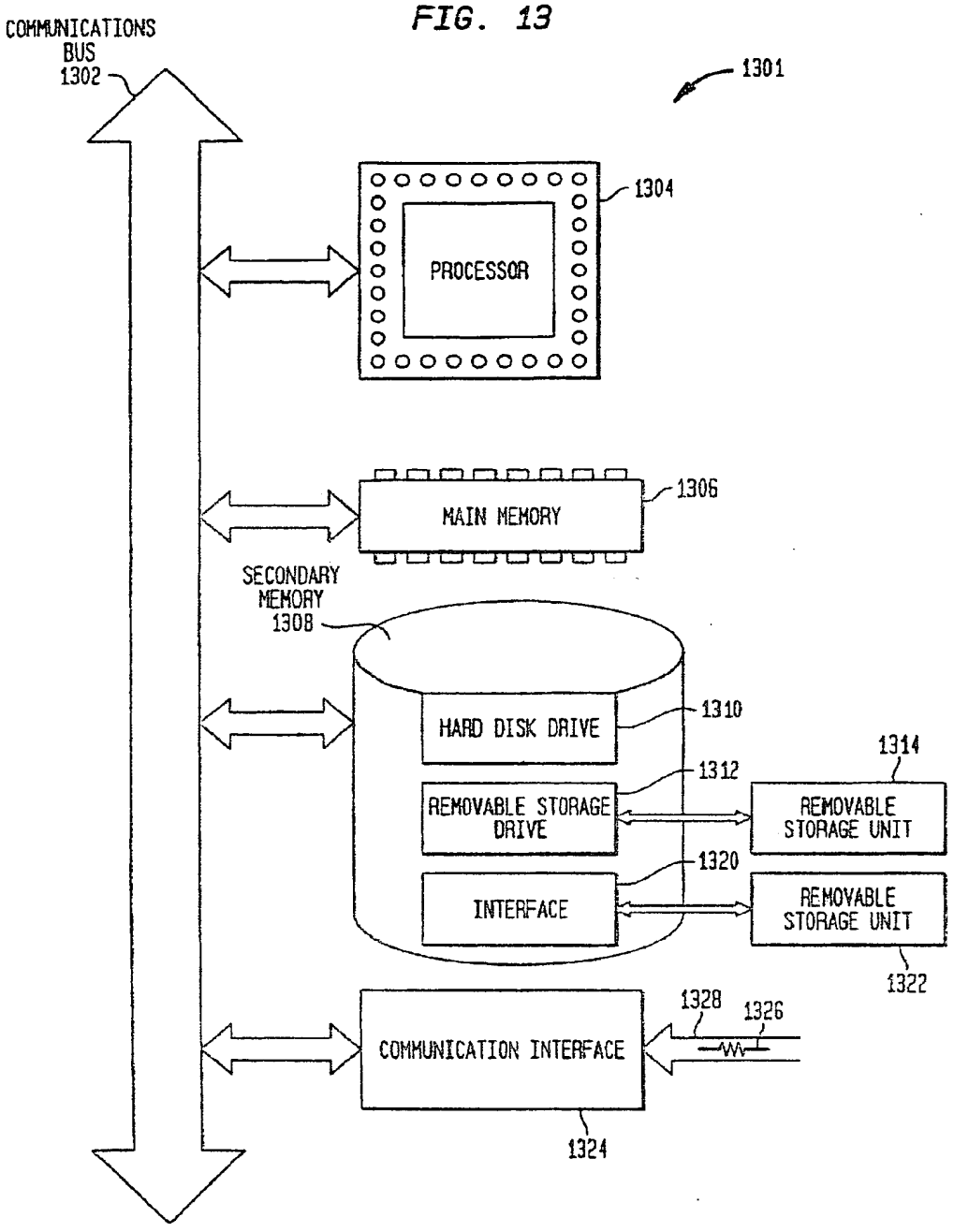

COMMUNICATIONS BUS
1302
1301
1304
PROCESSOR
1306
MAIN MEMORY
SECONDARY MEMORY
1308
HARD DISK DRIVE
1310
1312
REMOVABLE STORAGE DRIVE
1314
REMOVABLE STORAGE UNIT
1320
INTERFACE
REMOVABLE STORAGE UNIT
1322
1328
1326
COMMUNICATION INTERFACE
1324

FIG. 14A

	UNIT OPERATION TYPE	GROUP 1		
		PARAMETER	SOLN.	
T1	INNOCULUM PREP	NUMBER OF FLASKS		2
		MEDIA VOLUME/FLASK		0.25 LITERS
T2	FLASK GROWTH	SCALE UP RATIO		10 FOLD
		MEDIA VOLUME/FLASK		1.25 L
T3	FERMENTATION PRODUCTION	SCALE UP RATIO		10 FOLD
		FERMENTOR WORKING VOLUME	S-101	500 LITERS
		ANTIFOAM A	S-102	1 MI/L
		ANTIFOAM B	S-103	1 MI/L
		BASE	S-104	5 MI/L
		ACID	S-105	5 MI/L
T4	INITIAL SEEDING	NUMBER OF AMPULES		2
		VOLUME PER AMPULE		2 MI
		STARTING CELL DENSITY		300,000 CELLS/MI
		AMPULE SPLIT RATIO		1 VESSELS/AMPULE
		CULTURE VESSEL TYPE		ROLL. BOT.
		FEED VOLUME		100 MI
T5	CULTURE VESSEL SPLIT	VESSEL SPLIT RATIO		2
		NEW VESSEL TYPE		RB
		FEED VOLUME		100 MI
		SERUM CONTENT		2.0% FETAL BOVINE SERUM
T6	SPINNER FLASK SEEDING	FLASK FEED VOLUME		4 LITERS
		VESSEL/FLASK RATIO		0.1 L. CELLS/L FLASK
		uCARRIER DENSITY		5 Gm/LITER
		NUMBER OF PBS WASHES		2
		NUMBER OF MEDIA WASHES		1
		NO. OF MEDIA/SERUM WASHES		2 FBS
T7	BIOSYNTHESIS BIOREACTOR PREPARATION (STIRRED TANK REACTOR)	REACTOR FEED VOLUME		500 LITERS
		SPINNER/REACTOR RATIO		0.3
		uCARRIER DENSITY		5 Gm/LITER
		NUMBER OF PBS WASHES		2
		NUMBER OF MEDIA WASHES		1
		NO. OF MEDIA/SERUM WASHES		2
T8	BIOSYNTHESIS BIOREACTOR PREPARATION (HOLLOW FIBER REACTOR)	REACTOR FEED VOLUME		100 LITERS
		NUMBER OF PBS WASHES		2
		NUMBER OF MEDIA WASHES		2
		NO. OF MEDIA/SERUM WASHES		2
		SERUM CONTENT		2.0% FETAL BOVINE SERUM
T9	BIOSYNTHESIS BIOREACTOR PREPARATION (FLUIDIZED BED REACTOR)	REACTOR FEED VOLUME		LITERS
		uCARRIER DENSITY		Gms/L
		NUMBER OF PBS WASHES		
		NUMBER OF MEDIA WASHES		
		NO. OF MEDIA/SERUM WASHES		
		SERUM CONTENT		
T10	INITIAL SEEDING	NUMBER OF AMPULES		2
		VOLUME PER AMPULE		2 MI
		STARTING CELL DENSITY		300,000 CELLS/MI
		AMPULE SPLIT RATIO		1 VESSELS/AMPULE

FIG. 14B

GROUP 2			GROUP 3		
PARAMETER	SOLN.		PARAMETER	SOLN.	
TEMPERATURE AGITATION DURATION		37 C 200 RPM 18 HOURS	FINAL OD		12
TEMPERATURE AGITATION DURATION		37 C 200 HOURS 16 RPM	FINAL OD		12
GROWTH TEMPERATURE AGITATION SPARGE RATE BACK PRESSURE TOTAL DURATION		37 HOURS 1 HP/100L 1.5 VVM 5 PSIG 21 HRS	FINAL OD DRY CELL MASS PRODUCT CONCENTRATION CIP		12 9.96 Gcs TDCH/L 0.3 Gms PRODUCT/L Y
SERUM CONTENT FEED RATE DAYS TO CONFLUENCE		2.0% FETAL BOVINE SERUM 1 FEED PER VESSEL PER 2 DAYS 2 DAYS	AMPLIFICATION FACTOR		100%
FEED RATE DAYS TO CONFLUENCE		1 FEED PER VESSEL PER 2 DAYS 2 DAYS	AMPLIFICATION FACTOR		100%
SERUM CONTENT FEED RATE DAYS TO CONFLUENCE		2.0% FETAL BOVINE SERUM 1 FEED PER VESSEL PER 2 DAYS 2 DAYS	AMPLIFICATION FACTOR		100%
SERUM CONTENT FEED RATE DAYS TO CONFLUENCE SERUM FREE MEDIA WASHES		2.0% FETAL BOVINE SERUM 1 FEED PER VESSEL PER 2 DAYS 10 DAYS 2	PRODUCT CONCENTRATION TOTAL PROTEIN CONCEN.		2500% Mg PROD/L 0.125 Mg TP/MI
NUMBER OF REACTORS FEED RATE DAYS TO CONFLUENCE		1 1 FEED PER VESSEL PER 1 DAYS 10 DAYS	HARVEST VOLUME PRODUCT CONCENTRATION TOTAL PROTEIN CONCEN.		500% LITERS 25 Mg PROD/L 0.125 Mg TP/MI
NUMBER OF REACTORS FEED RATE DAYS TO CONFLUENCE		1 1 FEED PER VESSEL PER 1 DAYS 10 DAYS	PRODUCT CONCENTRATION TOTAL PROTEIN CONCEN.		2500% Mg PROD/L 0.125 Mg TP/MI
SERUM CONTENT FEED RATE DAYS TO CONFLUENCE		2.0% FETAL BOVINE SERUM 1 FEED PER VESSEL PER 2 DAYS 2 DAYS	AMPLIFICATION FACTOR		100%

FIG. 15A

	UNIT OPERATION TYPE	GROUP 1		
		PARAMETER	SOLN.	
		CULTURE VESSEL TYPE		ROLL. BOT.
		FEED VOLUME		100 ML
T11	CULTURE VESSEL SPLIT	VESSEL SPLIT RATIO		2
		NEW VESSEL TYPE		RB
		FEED VOLUME		100 ML
		SERUM CONTENT		2.0% FETAL BOVINE SERUM
T12	SPINNER FLASK SPLIT	FLASK FEED VOLUME		4 LITERS
		VESSEL/FLASK RATIO		0.1 L CELLS/L FLASK
		uCARRIER DENSITY		5 Gm/LITER
		NUMBER OF PBS WASHES		2
		NUMBER OF MEDIA WASHES		1
		NO. OF MEDIA/SERUM WASHES		2
T13	BIOSYNTHESIS BIOREACTOR PREPARATION (STIRRED TANK REACTOR)	REACTOR FEED VOLUME		500 LITERS
		SPINNER/REACTOR RATIO		8.3
		uCARRIER DENSITY		5 Gm/LITER
		NUMBER OF PBS WASHES		2
		NUMBER OF MEDIA WASHES		1
		NO. OF MEDIA/SERUM WASHES		2
T14	BIOSYNTHESIS BIOREACTOR PREPARATION (FLUIDIZED BED REACTOR)	REACTOR FEED VOLUME		LITERS
		uCARRIER DENSITY		GmS/L
		NUMBER OF PBS WASHES		
		NUMBER OF MEDIA WASHES		
		NO. OF MEDIA/SERUM WASHES		
		SERUM CONTENT		
T15	INITIAL COUPLING	FLASK FEED VOLUME		4 LITERS
		VESSEL/FLASK RATIO		0.1 L CELLS/L FLASK
		uCARRIER DENSITY		5 Gm/LITER
		NUMBER OF PBS WASHES		2
		NUMBER OF MEDIA WASHES		1
		NO. OF MEDIA/SERUM WASHES		2 FBS
T16	ADDITIONAL COUPLING	REACTOR FEED VOLUME		500 LITERS
		SPINNER/REACTOR RATIO		8.3
		uCARRIER DENSITY		5 Gm/LITER
		NUMBER OF PBS WASHES		2
		NUMBER OF MEDIA WASHES		1
		NO. OF MEDIA/SERUM WASHES		2
T17	PEPTIDE CLEAVAGE	REACTOR FEED VOLUME		100 LITERS
		NUMBER OF PBS WASHES		2
		NUMBER OF MEDIA WASHES		2
		NO. OF MEDIA/SERUM WASHES		2
		SERUM CONTENT		2.0% FETAL BOVINE SERUM
T18	TISSUE THAWING	CRUDE PRODUCT YEILD		25 Gm CRUDE PROD./Kg TISSUE
		ENVIRONMENTAL TEMPERATURE		25 C
		THAW DURATION		16 HOURS
T19	HOMOGENIZATION	CRUDE PRODUCT YEILD		25 Gm CRUDE PROD./Kg TISSUE
		LIQUID/SOLID RATIO		10 L SOLUTION/KG TISSUE
		HOMOGENIZATION TEMP.		4 C
		HOMOGENIZER TYPE		RS
		ENERGY INPUT		200 HP/100L/HR
		DURATION		4 HOURS
T20	LIQUID THAWING			

FIG. 15B

GROUP 2			GROUP 3		
PARAMETER	SOLN.		PARAMETER	SOLN.	
PBS WASHES		200 Ml			
TRYPSIN WASH		100 Ml			
FEED RATE		1 FEED PER VESSEL PER 2 DAYS	AMPLIFICATION FACTOR		100%
DAYS TO CONFLUENCE		2 DAYS			
PBS WASHES		200 Ml			
TRYPSIN WASH		100 Ml			
SERUM CONTENT		2.0% FETAL BOVINE SERUM	AMPLIFICATION FACTOR		100%
FEED RATE		1 FEED PER VESSEL PER 2 DAYS			
DAYS TO CONFLUENCE		2 DAYS			
SERUM CONTENT		2.0% FETAL BOVINE SERUM	PRODUCT CONCENTRATION		2500% Mg PROD/L
FEED RATE		1 FEED PER VESSEL PER 2 DAYS	TOTAL PROTEIN CONCEN.		0.125 Mg TP/Ml
DAYS TO CONFLUENCE		10 DAYS			
SERUM FREE MEDIA WASHES		2			
NUMBER OF REACTORS		1	PRODUCT CONCENTRATION		2500% Mg PROD/L
FEED RATE		1 FEED PER VESSEL PER 1 DAYS	TOTAL PROTEIN CONCEN.		0.125 Mg TP/Ml
DAYS TO CONFLUENCE		10 DAYS			
SERUM CONTENT		2.0% FETAL BOVINE SERUM	AMPLIFICATION FACTOR		100%
FEED RATE		1 FEED PER VESSEL PER 2 DAYS			
DAYS TO CONFLUENCE		2 DAYS			
SERUM CONTENT		2.0% FETAL BOVINE SERUM	PRODUCT CONCENTRATION		2500% Mg PROD/L
FEED RATE		1 FEED PER VESSEL PER 2 DAYS	TOTAL PROTEIN CONCEN.		0.125 Mg TP/Ml
DAYS TO CONFLUENCE		10 DAYS			
SERUM FREE MEDIA WASHES		2			
NUMBER OF REACTORS		1	HARVEST VOLUME		500% LITERS
FEED RATE		1 FEED PER VESSEL PER 1 DAYS	PRODUCT CONCENTRATION		25 Mg PROD/L
DAYS TO CONFLUENCE		10 DAYS	TOTAL PROTEIN CONCEN.		0.125 Mg TP/Ml
CONTAMINANT PROTEIN CONC.		100 Ga/L	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
CONTAMINANT PROTEIN CONC.		100 Ga/L	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
			AMPLIFICATION FACTOR		100%

FIG. 16A

	UNIT OPERATION TYPE	GROUP 1		
		PARAMETER	SOLN.	
T21	PRODUCT Ppt BY SOLIDS	REAGENT CONCENTRATION		1 M
T22	PRODUCT Ppt BY LIQUIDS	REAGENT CONCENTRATION		1 M
T23	CONTAINMENT Ppt BY SOLIDS	REAGENT CONCENTRATION		1 M
T24	CONTAINMENT Ppt BY LIQUIDS	REAGENT CONCENTRATION		1 M
T25	SOLIDS HARVEST TANGENTIAL FLOW MF	POROSITY AVERAGE FLUX RATE TOTAL THROUGHPUT FILTRATION TIME		0.2 MICRON 11 L/SF/HR AT 40 PSIG AT 4 C 400 LITERS/SF 1 HR
T26	CONTINUOUS CENTRIFUGATION SOLIDS HARVEST	SYSTEM VOID VOLUME		5 LITERS
T27	CONTINUOUS CENTRIFUGATION SUPERNATANT HARVEST	SYSTEM VOID VOLUME		6 LITERS
T28	DILUTION	SYSTEM VOID VOLUME		6 LITERS
T29	BATCH CENTRIFUGATION SOLIDS HARVEST	SYSTEM VOID VOLUME		6 LITERS

FIG. 16B

GROUP 2			GROUP 3		
PARAMETER	SOLN.		PARAMETER	SOLN.	
Kgas OF REAGENT/LITERS PRODUCT		0.25 Kg/L	STEP RECOVERY OF PRODUCT		95%
TEMPERATURE		4 C	STEP RECOVERY OF T.P.		95%
ADDITION TIME		0.5 HOURS			
ADDITIONAL MIX TIME		2 HOURS	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
LITERS REAGENT/LITERS PRODUCT		0.25 L/L	STEP RECOVERY OF PRODUCT		95%
TEMPERATURE		4 C	STEP RECOVERY OF T.P.		95%
ADDITION TIME		0.5 HOURS			
ADDITIONAL MIX TIME		2 HOURS	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
Kgas OF REAGENT/LITERS PRODUCT		0.25 Kg/L	STEP RECOVERY OF PRODUCT		95%
TEMPERATURE		4 C	STEP RECOVERY OF T.P.		95%
ADDITION TIME		0.5 HOURS			
ADDITIONAL MIX TIME		2 HOURS	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
LITERS REAGENT/LITERS PRODUCT		0.25 L/L	STEP RECOVERY OF PRODUCT		95%
TEMPERATURE		4 C	STEP RECOVERY OF T.P.		95%
ADDITION TIME		0.5 HOURS			
ADDITIONAL MIX TIME		2 HOURS	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
FLUSH		2 L/SF	STEP RECOVERY OF PRODUCT		95%
PRIME		2 L/SF	STEP RECOVERY OF T.P.		95%
CONCENTRATION FACTOR		10 FOLD			
WASH		0.5 L/SF	TEMPERATURE REGULATION		Y
REGENERATE		1 L/SF	CIP		Y
STORE		2 L/SF	SIP		Y
RCF		10,000 X G	STEP RECOVERY OF PRODUCT		95%
TIME		60 MINUTES	STEP RECOVERY OF T.P.		95%
VOLUME REDUCTION		30 X VOL. REDUCTION			
WASH VOLUME		0.2 X SYSTEM VOID VOLUME	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
RCF		10,000 X G	STEP RECOVERY OF PRODUCT		85%
TIME		30 MINUTES	STEP RECOVERY OF T.P.		0.3
VOLUME REDUCTION		0.062 VOL. REDUCTION			
WASH VOLUME		1.5 X SYSTEM VOID VOLUME	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
RCF		10,000 X G	STEP RECOVERY OF PRODUCT		95%
TIME		30 MINUTES	STEP RECOVERY OF T.P.		0.95
VOLUME REDUCTION		16 X VOL. REDUCTION			
WASH VOLUME		1.5 X SYSTEM VOID VOLUME	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
RCF		10,000 X G	STEP RECOVERY OF PRODUCT		95%
TIME		30 MINUTES	STEP RECOVERY OF T.P.		0.95

FIG. 17A

	UNIT OPERATION TYPE	GROUP 1 PARAMETER	SOLN.	
T30	BATCH CENTRIFUGATION SUPERNATANT HARVEST	SYSTEM VOID VOLUME		6 LITERS
T31	CELL DISRUPTION HIGH PRESS. HOMOGEN.	PRODUCT TEMPERATURE UTILITY TEMPERATURE VOID VOLUME		8 C 2 C 5 LITERS
T32	CELL DISRUPTION BEAD MILL	NUMBER OF PASSES BEAD SIZE VOID VOLUME FLOW RATE		2 0.5 LPM
T33	CELL DISRUPTION CHEMICAL LYSIS	REAGENT TEMPERATURE EXPOSURE TIME		0.5 M NaOH 4 C 2 HOURS
T34	MICROFILTRATION TANGENTIAL FLOW	POROSITY AVERAGE FLUX RATE TOTAL THROUGHPUT FILTRATION TIME		0.2 MICRON 50 L/SF/HR AT 40 PSIG AT 4 C 400 LITERS/SF 2 HR
T35	MICROFILTRATION DEAD END	POROSITY AVERAGE FLUX RATE TOTAL THROUGHPUT FILTRATION TIME		0.2 MICRON 50 L/SF/HR AT 40 PSIG AT 4 C 400 LITERS/SF 0.5 HR
T36	ULTRAFILTRATION CONCENTRATION/DILUTION	POROSITY AVERAGE FLUX RATE CONCENTRATION TIME		60 K NMWL 3 L/SF/HR AT 40 PSIG AT 4 C 2 HR.
T37	ULTRAFILTRATION FLOW DIALYSIS	POROSITY AVERAGE FLUX RATE		60 K NMWL 3 L/SF/HR AT 40 PSIG AT 4 C

FIG. 17B

GROUP 2			GROUP 3		
PARAMETER	SOLN.		PARAMETER	SOLN.	
VOLUME REDUCTION		16 X VOL. REDUCTION			
WASH VOLUME		1.5 X SYSTEM VOID VOLUME	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
RCF		10000 X G	STEP RECOVERY OF PRODUCT		95%
TIME		30 MINUTES	STEP RECOVERY OF T.P.		0.95
VOLUME REDUCTION		16 X VOL. REDUCTION			
WASH VOLUME		1.5 X SYSTEM VOID VOLUME	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
NUMBER OF PASSES		6 TIMES	RINSE		500% VOID VOLUMES
PRESSURE		12,000 PSI	STEP RECOVERY OF PRODUCT		95%
FLOW RATE		5 LPM	STEP RECOVERY OF T.P.		95%
TEMPERATURE INCREASE		1.8 DEGREES C/1,000 PSI	TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
			STEP RECOVERY OF PRODUCT		95%
			STEP RECOVERY OF T.P.		
			TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
LITERS REAGENT/Gm PRODUCT		0.4 L/Gm	STEP RECOVERY OF PRODUCT		95%
TITRATION		0 MI/LITER	STEP RECOVERY OF T.P.		
			TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
FLUSH		2.00 L/SF	STEP RECOVERY OF PRODUCT		95%
PRIME		2.00 L/SF	STEP RECOVERY OF T.P.		95%
WASH		0.50 L/SF			
SOLIDS		0.30% OF PRODUCT SOLUTION	TEMPERATURE REGULATION		Y
REGENERATE		1.00 L/SF	CIP		Y
STORE		2.00 L/SF	SIP		Y
FLUSH		0 L/SF	STEP RECOVERY OF PRODUCT		95%
PRIME		0 L/SF	STEP RECOVERY OF T.P.		0.95
WASH		0.5 L/SF			
SOLIDS		0.003 OF PRODUCT SOLUTION	TEMPERATURE REGULATION		N
REGENERATE		1 L/SF	CIP		N
STORE		2 L/SF	SIP		N
FLUSH		2.00 L/SF	STORE		2.00 L/SF
PRIME		2.00 L/SF	STEP RECOVERY OF PRODUCT		95%
WASH		0.50 L/SF	STEP RECOVERY OF T.P.		95%
DILUTE CONCENTRATE		10.0 FOLD	TEMPERATURE REGULATION		Y
SOLIDS		0.30% OF PRODUCT SOLUTION	CIP		Y
REGENERATE		1.00 L/SF	SIP		Y
FLUSH		2 L/SF	STORE		200% L/SF
PRIME		2.00 L/SF	STEP RECOVERY OF PRODUCT		95%
DIALYSIS BUFFER		5.0 X FEED STREAM VOLUME	STEP RECOVERY OF T.P.		95%
WASH		0.50 L/SF	TEMPERATURE REGULATION		Y

FIG. 18A

	UNIT OPERATION TYPE	GROUP 1		
		PARAMETER	SOLN.	
		DIALYSIS TIME		2 HR
T38	PROD. ADS. CHROMATOGRAPHY HPLC	COLUMN CAPACITY COLUMN OVERSIZE FACTOR COLUMN ASPECT RATIO MAX. LINEAR VELOCITY		10 Mg PROD./MI OF PACKING 1.5 FOLD 0.37 H/D 100 Cm/HR AT 45 PSIG AND 4 C
T39	PROD. ADS. CHROMATOGRAPHY MPLC	COLUMN CAPACITY COLUMN OVERSIZE FACTOR COLUMN ASPECT RATIO MAX. LINEAR VELOCITY		10 Mg PROD./MI OF PACKING 1.5 FOLD 0.37 H/D 100 Cm/HR AT 45 PSIG AND 4 C
T40	PROD. ADS. CHROMATOGRAPHY LPLC	COLUMN CAPACITY COLUMN OVERSIZE FACTOR COLUMN ASPECT RATIO MAX. LINEAR VELOCITY		10 Mg PROD./MI OF PACKING 1.5 FOLD 0.37 H/D 100 Cm/HR AT 45 PSIG AND 4 C
T41	CONT. ADS. CHROMATOGRAPHY HPLC	COLUMN CAPACITY COLUMN OVERSIZE FACTOR COLUMN ASPECT RATIO MAX. LINEAR VELOCITY		30 Mg CONT./MI OF PACKING 1.5 FOLD 0.37 H/D 100 Cm/HR AT 45 PSIG AND 4 C
T42	CONT. ADS. CHROMATOGRAPHY MPLC	COLUMN CAPACITY COLUMN OVERSIZE FACTOR COLUMN ASPECT RATIO MAX. LINEAR VELOCITY		10 Mg CONT./MI OF PACKING 1.5 FOLD 0.37 H/D 100 Cm/HR AT 45 PSIG AND 400% C
T43	CONT. ADS. CHROMATOGRAPHY LPLC	COLUMN CAPACITY COLUMN OVERSIZE FACTOR COLUMN ASPECT RATIO MAX. LINEAR VELOCITY		10 Mg CONT./MI OF PACKING 1.5 FOLD 0.37 H/D 100 Cm/HR AT 45 PSIG AND 4 C
T44	SIZE EXCL. CHROMATOGRAPHY HPLC	LOAD CAPACITY LENGTH MAX. LINEAR VELOCITY VOID VOLUME		5% OF TOTAL COLUMN VOLUME 100 Cm 100 Cm/HR AT 45 PSIG AND 4 C 25% COLUMN VOLUME
T45	SIZE EXCL. CHROMATOGRAPHY MPLC	LOAD CAPACITY LENGTH MAX. LINEAR VELOCITY VOID VOLUME		5% OF TOTAL COLUMN VOLUME 100 Cm 100 Cm/HR AT 45 PSIG AND 4 C 25% COLUMN VOLUME

FIG. 18B

GROUP 2			GROUP 3		
PARAMETER	SOLN.		PARAMETER	SOLN.	
SOLIDS		0.30% OF PRODUCT SOLUTION	CIP		Y.
REGENERATE		1.00 L/SF	SIP		Y
COLUMN EQUILIBRATION		5 COLUMN VOLUMES	PROD. ELUTION VOLUME		80%
COLUMN WASH		3 COLUMN VOLUMES	STEP RECOVERY OF PRODUCT		95%
COLUMN ELUTE A		3 COLUMN VOLUMES	STEP RECOVERY OF T.P.		95%
COLUMN ELUTE B		0 COLUMN VOLUMES	TEMPERATURE REGULATION		N
COLUMN REGENERATE		1 COLUMN VOLUMES	CIP		Y
COLUMN STORE		2 COLUMN VOLUMES	SIP		Y
COLUMN EQUILIBRATION		5 COLUMN VOLUMES	PROD. ELUTION VOLUME		80%
COLUMN WASH		3 COLUMN VOLUMES	STEP RECOVERY OF PRODUCT		95%
COLUMN ELUTE A		3 COLUMN VOLUMES	STEP RECOVERY OF T.P.		95%
COLUMN ELUTE B		0 COLUMN VOLUMES	TEMPERATURE REGULATION		N
COLUMN REGENERATE		1 COLUMN VOLUMES	CIP		Y
COLUMN STORE		2 COLUMN VOLUMES	SIP		Y
COLUMN EQUILIBRATION		5 COLUMN VOLUMES	PROD. ELUTION VOLUME		42%
COLUMN WASH		3 COLUMN VOLUMES	STEP RECOVERY OF PRODUCT		95%
COLUMN ELUTE A		3 COLUMN VOLUMES	STEP RECOVERY OF T.P.		95%
COLUMN ELUTE B		2 COLUMN VOLUMES	TEMPERATURE REGULATION		N
COLUMN REGENERATE		1 COLUMN VOLUMES	CIP		Y
COLUMN STORE		2 COLUMN VOLUMES	SIP		Y
COLUMN EQUILIBRATION		5 COLUMN VOLUMES	PROD. ELUTION VOLUME		42%
COLUMN WASH		3 COLUMN VOLUMES	STEP RECOVERY OF PRODUCT		95%
COLUMN ELUTE A		3 COLUMN VOLUMES	STEP RECOVERY OF T.P.		95%
COLUMN ELUTE B		2 COLUMN VOLUMES	TEMPERATURE REGULATION		N
COLUMN REGENERATE		1 COLUMN VOLUMES	CIP		Y
COLUMN STORE		2 COLUMN VOLUMES	SIP		Y
COLUMN EQUILIBRATION		5 COLUMN VOLUMES	PROD. ELUTION VOLUME		42%
COLUMN WASH		3 COLUMN VOLUMES	STEP RECOVERY OF PRODUCT		95%
COLUMN ELUTE A		3 COLUMN VOLUMES	STEP RECOVERY OF T.P.		95%
COLUMN ELUTE B		2 COLUMN VOLUMES	TEMPERATURE REGULATION		N
COLUMN REGENERATE		1 COLUMN VOLUMES	CIP		Y
COLUMN STORE		2 COLUMN VOLUMES	SIP		Y
COLUMN EQUILIBRATION		5 COLUMN VOLUMES	PROD. ELUTION VOLUME		42% COLUMNS VOLUMES
COLUMN WASH		3 COLUMN VOLUMES	STEP RECOVERY OF PRODUCT		95%
COLUMN ELUTE A		3 COLUMN VOLUMES	STEP RECOVERY OF T.P.		95%
COLUMN ELUTE B		2 COLUMN VOLUMES	TEMPERATURE REGULATION		N
COLUMN REGENERATE		1 COLUMN VOLUMES	CIP		Y
COLUMN STORE		2 COLUMN VOLUMES	SIP		Y
COLUMN EQUILIBRATION		4 COLUMN VOLUMES	PROD. ELUTION VOLUME		42% COLUMNS VOLUMES
COLUMN WASH		1 COLUMN VOLUMES	STEP RECOVERY OF PRODUCT		95%
COLUMN REGENERATE		1 COLUMN VOLUMES	STEP RECOVERY OF T.P.		95%
COLUMN STORE		2 COLUMN VOLUMES	TEMPERATURE REGULATION		N
			CIP		Y
			SIP		Y
COLUMN EQUILIBRATION		4 COLUMN VOLUMES	PROD. ELUTION VOLUME		42% COLUMNS VOLUMES
COLUMN WASH		1 COLUMN VOLUMES	STEP RECOVERY OF PRODUCT		95%
COLUMN REGENERATE		1 COLUMN VOLUMES	STEP RECOVERY OF T.P.		95%
COLUMN STORE		2 COLUMN VOLUMES	TEMPERATURE REGULATION		N
			CIP		Y
			SIP		Y

FIG. 19A

	UNIT OPERATION TYPE	GROUP 1		
		PARAMETER	SOLN.	
T46	SIZE EXCL. CHROMATOGRAPHY LPLC	LOAD CAPACITY		5% OF TOTAL COLUMN VOLUME
		LENGTH		100 Cm
		MAX. LINEAR VELOCITY		100 Cm/HR AT
				45 PSIG AND
				4 C
		VOID VOLUME		25% COLUMN VOLUME
T47	DILUTION	DILUTION FACTOR		3 LITERS/LITER
T48	RESOLUBILIZATION	REGEANT/PRODUCT RATIO		0 L/Kg PRODUCT
		DISSOLUTION TIME		0.50 HOURS
		ADDITIONAL MIX TIME		0.50 HOURS
T49	ENZYMATIC MODIFICTAION	ENZYME TO PRODUCT RATIO		0.084 LITERS OF ENZYME STOCK PER LITER OF START. PROC. VOL.
		ENZYME CONCENTRATION		2 Mg/Ml
		REACTION TEMP.		37 DEGREES C
		REACTION DURATION		30 MINUTES
				100%
T50	LYOPHILIZATION	PRODUCT CAPACITY/LOAD		8 UNITS
		PRODUCT UNIT SIZE		100 GRAMS/UNIT
T51	HEAT EXCHANGE	PROCESS INITIAL TEMP		98.6 DEGREES C
		PROCESS FINAL TEMP		39.2 DEGREES C
		UTILITY INITIAL TEMP		34 DEGREES C
		UTILITY FINAL TEMP		5 DEGREES C
		PROCESS SPECIFIC HEAT		38.6 K BTU/HR
		DESIGN TYPE (P,T,C)		P
T52	STORAGE			
T53	FERMENTATION SEED	SCALE UP RATIO		10 FOLD
		FERMENTOR WORKING VOLUME		50 LITERS
		ANTIFOAM A		1 Ml/L
		ANTIFOAM B		1 Ml/L
		BASE		5 Ml/L
		ACID		5 Ml/L
T54	INITIAL SEEDING	FLASK FEED VOLUME		12 LITERS
		SPINNER SPLIT RATIO		4

FIG. 19B

GROUP 2			GROUP 3		
PARAMETER	SOLN.		PARAMETER	SOLN.	
COLUMN EQUILIBRATION		4 COLUMN VOLUMES	PROD. ELUTION VOLUME		42% COLUMN VOLUMES
COLUMN WASH		1 COLUMN VOLUMES	STEP RECOVERY OF PRODUCT		95%
COLUMN REGENERATE		1 COLUMN VOLUMES	STEP RECOVERY OF T.P.		95%
COLUMN STORE		2 COLUMN VOLUMES	TEMPERATURE REGULATION		N
			CIP		Y
			SIP		Y
DILUTION TIME		0.5 HOURS	STEP RECOVERY OF PRODUCT		95%
ADDITIONAL MIX TIME		1 HOURS	STEP RECOVERY OF T.P.		95%
			TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
REGEANT 1		WATER	STEP RECOVERY OF PRODUCT		95%
CONCENTRATION		DIST.	STEP RECOVERY OF T.P.		95%
			TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
TITRATION SOLUTION-1		0.067 L/L PROCESS	STEP RECOVERY OF PRODUCT		95%
TITRATION SOLUTION-2		0.02 L/L PROCESS	STEP RECOVERY OF T.P.		95%
NEUTRALIZATION		0.57 L/L PROCESS			
			TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
LYOPHILIZATION TIME		18 HOURS	STEP RECOVERY OF PRODUCT		95%
PRODUCT WEIGHT REDUCTION		0.95	STEP RECOVERY OF T.P.		95%
					Y
			CIP		Y
			SIP		Y
EXPOSURE TIME		1 HOURS	STEP RECOVERY OF PRODUCT		100%
			STEP RECOVERY OF T.P.		100%
			TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
			STEP RECOVERY OF PRODUCT		95%
			STEP RECOVERY OF T.P.		95%
			TEMPERATURE REGULATION		Y
			CIP		Y
			SIP		Y
GROWTH TEMPERATURE		37 HOURS	FINAL OD		12
AGITATION		1 HP/100L	CIP		
SPARGE RATE		1.5 VVM			
BACK PRESSURE		5 PSIG			Y
TOTAL DURATION		21 HRS			
SERUM CONTENT		2% FBS	AMPLIFICATION FACTOR		1
FEED RATE		1 FEED PER VESSEL PER			

FIG. 20A

	UNIT OPERATION TYPE	GROUP 1		
		PARAMETER	SOLN.	
		uCARRIER DENSITY		5 Gm/LITER
		NUMBER OF PBS WASHES		2
		NUMBER OF MEDIA WASHES		1
		NO. OF MEDIA/SERUM WASHES		2 FBS
T55	CULTURE VESSEL SPLIT	FLASK FEED VOLUME		12 LITERS
		SPINNER SPLIT RATIO		4
		uCARRIER DENSITY		5 Gm/LITER
		NUMBER OF PBS WASHES		2
		NUMBER OF MEDIA WASHES		1
		NO. OF MEDIA/SERUM WASHES		2 FBS
T56	CULTURE FLASK SPLIT			
T57	STIRRED TANK REACTOR			
T58	FLUIDIZED BED REACTOR	PROCESS INITIAL TEMP		37 DEGREES C
		PROCESS FINAL TEMP		4 DEGREES C
		UTILITY INITIAL TEMP		2 DEGREES C
		UTILITY FINAL TEMP		5 DEGREES C
		PROCESS SPECIFIC HEAT		12 K BTU/HR
		DESIGN TYPE (P,T,C)		P
T59	LIQUID/LIQUID EXTRACTION	LIQUID/LIQUID RATIO		1 L EXTRACTION/L PRODUCT
		EXTRACTION TEMPERATURE		4 C
		ADDITION DURATION		0.5 HOURS
		ADDITIONAL MIX. DURATION		4 HOURS
		MIX ENERGY		0.3 HP/100L
T60	SOLID/LIQUID EXTRACTION	LIQUID/LIQUID RATIO		1 L EXTRACTION/L PRODUCT
		EXTRACTION TEMPERATURE		4 C
		DURATION		4 HOURS
		MIX ENERGY		0.3 HP/100 L

FIG. 20B

GROUP 2			GROUP 3		
PARAMETER	SOLN.		PARAMETER	SOLN.	
DAYS TO CONFLUENCE		2 DAYS 2 DAYS			
SERUM CONTENT FEED RATE DAYS TO CONFLUENCE		2% FBS 1 FEED PER VESSEL PER 2 DAYS 2 DAYS	AMPLIFICATION FACTOR		1
			STEP RECOVERY OF PRODUCT STEP RECOVERY OF T.P. CIP SIP		0.95 95% Y Y Y
EXPOSURE TIME		50% HOURS	STEP RECOVERY OF PRODUCT STEP RECOVERY OF T.P. TEMPERATURE REGULATION CIP SIP		0.95 100% Y Y Y
PHASE SEPARATION TIME PRODUCT PHASE (TOP/BOTTOM) HARVEST TIME		1600% HOURS TOP 0.5 HOURS	STEP RECOVERY OF PRODUCT STEP RECOVERY OF T.P. TEMPERATURE REGULATION CIP SIP		0.9 50% Y Y Y
PHASE SEPARATION TIME PRODUCT PHASE (TOP/BOTTOM) HARVEST TIME		1500% HOURS TOP 0.5 HOURS	STEP RECOVERY OF PRODUCT STEP RECOVERY OF T.P. TEMPERATURE REGULATION CIP SIP		0.9 50% Y Y Y

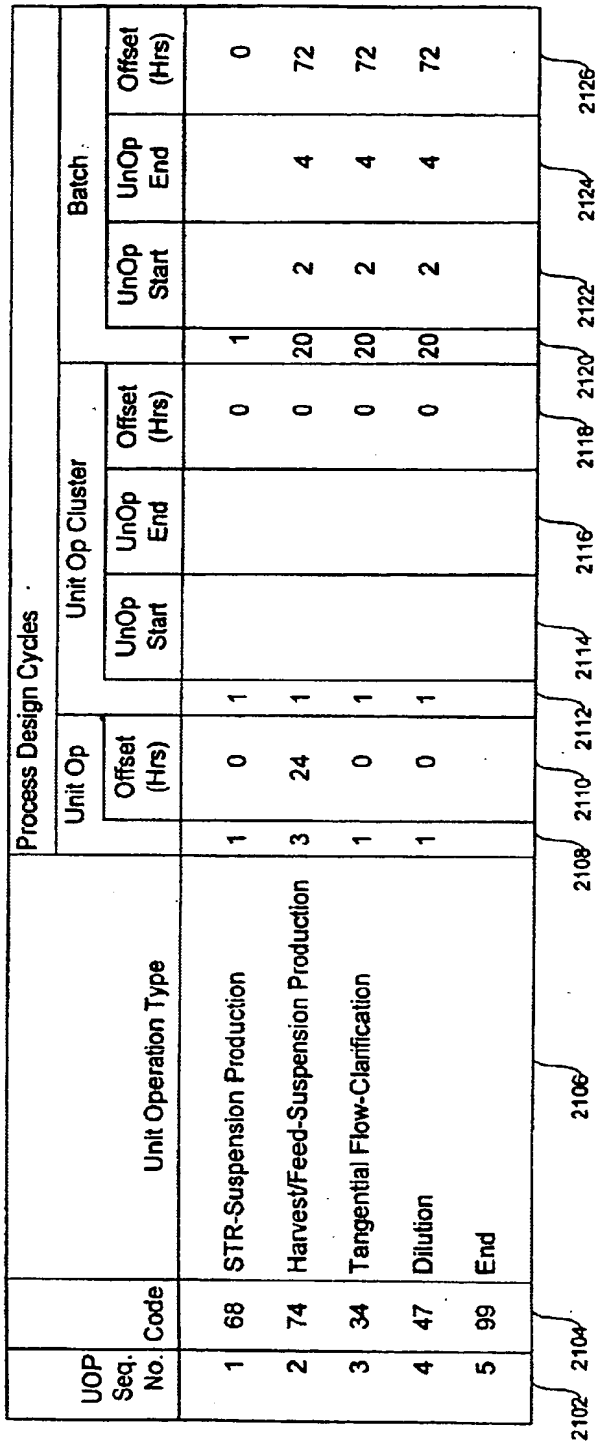

Process Design Cycles
UOP Seq. No.
Code
Unit Operation Type
Unit Op
Offset (Hrs)
Unit Op Cluster
UnOp Start
UnOp End
Offset (Hrs)
Batch
UnOp Start
UnOp End
Offset (Hrs)
1 68 STR-Suspension Production 1 0 1 0 1 0
2 74 Harvest/Feed-Suspension Production 3 24 1 0 20 2 4 72
3 34 Tangential Flow-Clarification 1 0 1 0 20 2 4 72
4 47 Dilution 1 0 1 0 20 2 4 72
5 99 End
2102
2104
2106
2108
2110
2112
2114
2116
2118
2120
2122
2124
2126

FIG. 21

UOP Seq. No.	Code	Unit Operation Type	Process Design Cycles								
			Unit Op		Unit Op Cluster				Batch		
				Offset (Hrs)		UnOp Start	UnOp End	Offset (Hrs)		UnOp Start	UnOp End	Offset (Hrs)
10301	87	Pool	1		1				1			
10302	51	Heat Exchange	1		1				1			
10303	26	Cont. Centrifugation - Solids Harvest	1		1				1			
10304	48	Resolubilization	1		1				1			
10305	61	Inlet Heat Exchange	1		3	5	7		1			
10306	31	High Pressure Homogenization	1		3	5	7	S	1			
10307	51	Outlet Heat Exchange	1		3	5	7	S	1			
10308	29	Batch Centrifugation - Solids Harvest	1		1				1			
10309	29	Dilution - IB Wash	1		2	9	10		1			
10310	29	Batch Centrifugation - Solids Harvest	1		2	9	10		1			
10311	63	Storage	1		1				1			
10312	99	End	1		1				1			

2202 2204 2206 2208 2210 2212 2214 2216 2218 2220 2222 2224 2226

FIG. 22

OPERATION	CALCULATIONS					
1.1.1.1 T76 MULTI-STAGE POOL	LINK SOURCE					
SET UP						
INPUT 1	PE-0102e	20272.98 LITERS @	104.00 HOURS, TRANSFER IN	0.0 HOURS=	0.0 LPM	
INPUT 2		0 LITERS @	0.00 HOURS, TRANSFER IN	0.0 HOURS=	0.0 LPM	
INPUT 3		0 LITERS @	0.00 HOURS, TRANSFER IN	0.0 HOURS=	0.0 LPM	
INPUT 4		0 LITERS @	0.00 HOURS, TRANSFER IN	0.0 HOURS=	0.0 LPM	
INPUT 5		0 LITERS @	0.00 HOURS, TRANSFER IN	0.0 HOURS=	0.0 LPM	
INPUT 6		0 LITERS @	0.00 HOURS, TRANSFER IN	0.0 HOURS=	0.0 LPM	
POOL INPUTS		20272.98 LITERS IN	0.00 HOURS, TRANSFER IN	0.0 HOURS=	0.0 LPM	
SUB TOTAL			104.00 TOTAL TRANSFER	0 HOURS	LPM MISC.	
2.1.1.1 51 OUTLET HEAT EXCHANGE						
SET UP						
TRANSFER	20,273.0 L IN	2.50 HRS =	135.2 LPM			
WASH						
CIP						
SIP						
CLEAN UP						
SUB TOTAL			135.2			
3.1.1.1 26 CONT. CERT/SOLIDS						
SET UP						
CENTRIFUGATION	20,273.0 L IN	5.00 HRS =	56.3 LPM			
WASH	30.0 L IN	0.01 HRS =	56.3 LPM			
CIP						
SIP						
CLEAN UP						
SUB TOTAL			56.3 LPM			
4.1.1.1 48 RESOLUBILIZATION						
SET UP						
DILUTION	6,476.0 L IN	3.0 HOURS	38.0 LPM			
WO		0.0 HOURS				
CIP						
SIP						
CLEAN UP						
SUB TOTAL			36.0			
5.1.1.1 61 INLET HEAT EXCHANGE						
SET UP						
TRANSFER	8,634.7 L IN	2.5 HRS =	57.56 LPM			
WASH	0.0 L IN	0.0 HRS =	0.0 LPM			

2302 2304

FIG.23A-1

PROCESS TIME LINE													
DURATION (HRS)			REL. TIME SCALE (HRS)			ABS. HOURS		ABS. DAYS		START		FINISH	
CALC.	LOG	ADJ.	PREP	EXEC.	COMPL.	START	END	START	END	DATE	TIME	DATE	TIME
0.0	0.0	0.0 HRS	104.0			104.0	104.0	4.33	4.33	01/08/99	06:00 AM	01/08/99	08:00 AM
0.0	0.0	0.0 HRS		104.0		104.0	104.0	4.33	4.33	01/08/99	06:00 AM	01/08/99	08:00 AM
0.0	0.0	0.0 HRS				0.0	0.0	0.00	0.00				
0.0	0.0	0.0 HRS				0.0	0.0	0.00	0.00				
0.0	0.0	0.0 HRS				0.0	0.0	0.00	0.00				
0.0	0.0	0.0 HRS				0.0	0.0	0.00	0.00				
0.0	0.0	0.0 HRS				0.0	0.0	0.00	0.00				
0.0	0.0	0.0 HRS				0.0	0.0	0.00	0.00				
0.0	0.0	0.0 HRS				0.0	0.0	0.00	0.00				
0.0	0.0	0.0 HRS		104.0		104.0	104.0	4.33	4.33	01/08/99	06:00 AM	01/08/99	08:00 AM
0.0		0.0 HRS		104.0			0.0			01/08/99	06:00 AM	01/08/99	08:00 AM
										HRS/CY	0.0		
										OK			
1.0	0.0	1.0 HRS	104.0			103.0	104.0	4.28	4.33	01/08/99	07:00 AM	01/08/99	08:00 AM
2.50	0.0	2.5 HRS		106.5		104.0	106.5	4.33	4.44	01/08/99	08:00 AM	01/08/99	10:30 AM
0.63	0.0	0.5 HRS		107.1		106.5	107.1	4.44	4.46	01/08/99	10:30 AM	01/08/99	11:07 AM
0.0	0.0	0.0 HRS			107.1	107.1	107.1	4.46	4.46	01/08/99	11:07 AM	01/08/99	11:07 AM
0.0	0.0	0.0 HRS			107.1	107.1	107.1	4.46	4.46	01/08/99	11:07 AM	01/08/99	11:07 AM
2.0	0.0	2.0 HRS			109.1	107.1	109.1	4.46	4.55	01/08/99	11:07 AM	01/08/99	01:07 PM
5.1		5.1 HRS		106.5						01/08/99	07:00 AM	01/08/99	01:07 PM
										HRS/CY	5.1		
										OK			
1.0	0.0	1.0 HRS	105.6			105.6	106.5	4.00	4.44	01/08/99	09:30 AM	01/08/99	10:30 AM
6.0	0.0	6.0 HRS		112.5		106.5	112.5	4.64	4.64	01/08/99	10:30 AM	01/08/99	04:30 PM
0.0	0.0	0.0 HRS		112.5		112.5	112.5	4.68	4.68	01/08/99	04:10 PM	01/08/99	04:30 PM
0.0	0.0	0.0 HRS			112.5	112.5	112.5	4.68	4.68	01/08/99	04:10 PM	01/08/99	04:30 PM
0.0	0.0	0.0 HRS			112.5	112.5	112.5	4.68	4.68	01/08/99	04:30 PM	01/08/99	04:30 PM
0.0	0.0	0.0 HRS			112.5	112.5	112.5	4.68	4.68	01/08/99	04:30 PM	01/08/99	04:30 PM
7.0		7.0 HRS		112.5			112.5			01/08/99	09:30 AM	01/08/99	04:30 PM
										HRS/CY	3.0		
										OK			
1.0	0.0	1.0 HRS	112.6			111.0	112.0	4.85	4.68	01/08/99	03:30 PM	01/08/99	04:30 PM
3.00	0.0	3.0 HRS		115.5		112.5	115.5	4.88	4.81	01/08/99	04:30 PM	01/08/99	07:30 PM
0.00	0.0	0.0 HRS		115.5		115.5	115.5	4.81	4.81	01/08/99	07:30 PM	01/08/99	07:30 PM
0.0	0.0	0.0 HRS			115.5	115.5	115.5	4.81	4.81	01/08/99	07:30 PM	01/08/99	07:30 PM
0.00	0.0	0.0 HRS			115.5	115.5	115.5	4.81	4.81	01/08/99	07:30 PM	01/08/99	07:30 PM
1.00	0.0	1.0 HRS			116.5	115.5	118.5	4.81	4.85	01/08/99	07:30 PM	01/08/99	08:30 PM
5.00		5.00 HRS		115.5						01/08/99	03:30 PM	01/08/99	08:30 PM
										HRS/CY	5.0		
										OK			
1.0	0.0	1.0 HRS	115.5			114.5	115.5	4.77	4.81	01/08/99	06:30 PM	01/08/99	07:30 PM
2.50	0.0	2.5 HRS		118.0		115.5	118.0	4.81	4.92	01/08/99	07:30 PM	01/08/99	10:00 PM
0.00	0.0	0.0 HRS		118.0		118.0	118.0	4.92	4.92	01/08/99	10:00 PM	01/08/99	10:00 PM

2306 2308 2310 2312 2314 2316 2318 2320 2322 2324 2326 2328 2330

FIG. 23A-2

OPERATION	CALCULATIONS			
CIP				
SIP				
CLEAN UP				
SUB TOTAL			57.6	
6.1.1.1 31 HOMOGENIZATION				
SET UP				
LYOS	3834.7 L IN	2.5 HRS	=	57.6 LPM
WASH	0.0 L IN	0.0 HRS	=	0.0 LPM
CIP				
SIP				
CLEAN UP				
SUB TOTAL			57.564344	
7.1.1.1 51 OUTLET HEAT EXCHANGE				
SET UP				
TRANSFER	3543.7 L IN	2.5 HRS	=	57.58 LPM
WASH	0.0 L IN	0.0 HRS	=	0.0 LPM
CIP				
SIP				
CLEAN UP				
SUB TOTAL			57.56	
5.1.2.1 61 INLET HEAT EXCHANGE				
SET UP				
TRANSFER	8634.7 L IN	2.5 HRS	=	57.56 LPM
WASH	0.0 L IN	0.0 HRS	=	0.0 LPM
CIP				
SIP				
CLEAN UP				
SUB TOTAL				
6.1.2.1 31 HOMOGENIZATION				
SET UP				
DILUTION	6834.7 L IN	2.5 HRS	=	57.6 LPM
WO	0.0 L IN	0.0 HRS	=	0.0 LPM
CIP				
SIP				
CLEAN UP				
SUB TOTAL			57.56	
7.1.2.1 51 OUTLET HEAT EXCHANGE				

FIG.23B-1

PROCESS TIME LINE													
DURATION (HRS)			REL. TIME SCALE (HRS)			ABS. HOURS		ABS. DAYS		START		FINISH	
CALC.	LOG	ADJ.	PREP	EXEC.	COMPL.	START	END	START	END	DATE	TIME	DATE	TIME
0.0	0.0	0.0 HRS			118.0	118.0	118.0	4.92	4.92	01/08/99	10:00 PM	01/08/99	10:00 PM
0.0	0.0	0.0 HRS			118.0	118.0	118.0	4.92	4.92	01/08/99	10:00 PM	01/08/99	10:00 PM
0.0	0.0	0.0 HRS			118.0	118.0	118.0	4.92	4.92	01/08/99	10:00 PM	01/08/99	10:00 PM
2.5		2.5 HRS		116.0						01/08/99	06:30 PM	01/08/99	10:00 PM
										HRS/CY	3.5		
										OK			
1.0	0.0	1.0 HRS	118.0			117.0	118.0	4.88	4.92	01/08/99	08:00 AM	01/08/99	10:00 PM
2.5	0.0	2.5 HRS		120.5		118.0	120.5	4.92	5.02	01/08/99	10:00 PM	01/08/99	12:30 AM
0.00	0.0	0.0 HRS		120.5		120.5	120.5	5.02	5.02	01/08/99	12:30 AM	01/08/99	12:30 AM
0.0	0.0	0.0 HRS			120.5	120.5	120.5	5.02	5.02	01/08/99	12:30 AM	01/08/99	12:30 AM
0.0	0.0	0.0 HRS			120.5	120.5	120.5	5.02	5.02	01/08/99	12:30 AM	01/08/99	12:30 AM
0.0	0.0	0.0 HRS			120.5	120.5	120.5	5.02	5.02	01/08/99	12:30 AM	01/08/99	12:30 AM
3.5		3.5 HRS		120.5			120.5			01/08/99	09:00 PM	01/08/99	12:30 AM
										HRS/CY	3.5		
										OK			
1.0	0.0	1.0 HRS	120.5			118.5	120.0	4.88	5.02	01/08/99	11:30 PM	01/08/99	12:30 AM
2.50	0.0	2.5 HRS		123.0		120.5	123.0	5.02	5.13	01/08/99	12:30 AM	01/08/99	03:00 AM
0.00	0.0	0.0 HRS		123.0		123.0	123.0	5.13	5.13	01/08/99	03:00 AM	01/08/99	03:00 AM
0.0	0.0	0.0 HRS			123.0	123.0	123.0	5.13	5.13	01/08/99	03:00 AM	01/08/99	03:00 AM
0.0	0.0	0.0 HRS			123.0	123.0	123.0	5.13	5.13	01/08/99	03:00 AM	01/08/99	03:00 AM
0.0	0.0	0.0 HRS			123.0	123.0	123.0	5.13	5.13	01/08/99	03:00 AM	01/08/99	03:00 AM
2.5		2.5 HRS		123.0						01/08/99	11:30 PM	01/08/99	03:00 AM
										HRS/CY	3.5		
										OK			
0.0	0.0	0.0 HRS	123.0			123.0	123.0	5.13	5.13	01/08/99	03:00 AM	01/08/99	03:00 AM
2.50	0.0	2.5 HRS		125.5		123.0	125.5	5.13	5.23	01/08/99	03:00 AM	01/08/99	05:30 AM
0.00	0.0	0.0 HRS		125.5		125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
0.0	0.0	0.0 HRS			125.5	125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
0.0	0.0	0.0 HRS			125.5	125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
0.0	0.0	0.0 HRS			125.5	125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
2.5		2.5 HRS		125.5 01F895						01/08/99	03:00 AM	01/08/99	05:30 AM
										HRS/CY	2.5		
										OK			
1.0	0.0	0.0 HRS	123.0			123.0	123.0	5.13	5.13	01/08/99	03:00 AM	01/08/99	03:00 AM
2.5	0.0	2.5 HRS		125.5		123.0	125.5	5.13	5.23	01/08/99	03:00 AM	01/08/99	05:30 AM
0.00	0.0	0.0 HRS		125.5		125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
0.0	0.0	0.0 HRS			125.5	125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
0.0	0.0	0.0 HRS			125.5	125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
0.0	0.0	0.0 HRS			125.5	125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
2.5		2.5 HRS		125.5			125.5			01/08/99	03:00 AM	01/08/99	05:30 AM
										HRS/CY	2.5		
										OK			

FIG.23B-2

	OPERATION	CALCULATIONS			
	SET UP				
	TRANSFER	8543.7 L IN	2.5 HRS	=	57.56 LPM
	WASH	0.0 L IN	0.0 HRS	=	0.0 LPM
	CIP				
	SIP				
	CLEAN UP				
	SUB TOTAL				
5.1.3.1 61	INLET HEAT EXCHANGE				
	SET UP				
	TRANSFER	8634.7 L IN	2.5 HRS	=	57.58 LPM
	WASH	9.0 L IN	0.0 HRS	=	57.6 LPM
	CIP				
	SIP				
	CLEAN UP				
	SUB TOTAL				
6.1.3.1 31	HOMOGENIZATION				
	SET UP				
	LYCIS	8634.7 L IN	2.5 HRS	=	57.6 LPM
	WASH	9.0 L IN	0.0 HRS	=	57.6 LPM
	CIP				
	SIP				
	CLEAN UP				
	SUB TOTAL				57.56 LPM
7.1.3.1 51	OUTLET HEAT EXCHANGE				
	SET UP				
	TRANSFER	8643.7 L IN	2.5 HRS	=	57.50 LPM
	WASH	9.0 L IN	0.0 HRS	=	57.6 LPM
	CIP				
	SIP				
	CLEAN UP				
	SUB TOTAL				

FIG.23C-1

PROCESS TIME LINE													
DURATION (HRS)			REL. TIME SCALE (HRS)			ABS. HOURS		ABS. DAYS		START		FINISH	
CALC.	LOG	ADJ.	PREP	EXEC.	COMPL.	START	END	START	END	DATE	TIME	DATE	TIME
0.0	0.0	0.0 HRS	123.0			123.0	123.0	5.13	5.13	01/08/99	03:00 AM	01/08/99	03:00 AM
2.50	0.0	2.5 HRS		125.5		123.0	125.5	5.13	5.23	01/08/99	03:00 AM	01/08/99	05:30 AM
0.00	0.0	0.0 HRS		125.5		125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
0.0	0.0	0.0 HRS			125.5	125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
0.0	0.0	0.0 HRS			125.5	125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
0.0	0.0	0.0 HRS			125.5	125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
2.5		2.5 HRS		125.5						01/08/99	03:00 AM	01/08/99	05:30 AM
										HRS/CY	2.5		
										OK			
0.0	0.0	0.0 HRS	125.5			125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
2.50	0.0	2.5 HRS		128.0		125.5	128.0	5.33	5.33	01/08/99	05:30 AM	01/08/99	08:00 AM
0.0	0.0	0.0 HRS		128.0		128.0	128.0	5.33	5.33	01/08/99	08:00 AM	01/08/99	08:01 AM
0.0	0.0	0.0 HRS			128.0	128.0	128.0	5.33	5.33	01/08/99	08:01 AM	01/08/99	08:01 AM
0.0	0.0	0.0 HRS			128.0	128.0	128.0	5.33	5.33	01/08/99	08:01 AM	01/08/99	08:01 AM
0.0	0.0	0.0 HRS			128.0	128.0	128.0	5.33	5.33	01/08/99	08:01 AM	01/08/99	08:01 AM
2.5		2.5 HRS		128.0						01/08/99	05:30 AM	01/08/99	08:01 AM
										HRS/CY	2.5		
										OK			
0.0	0.0	0.0 HRS	125.5			125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
2.5	0.0	2.5 HRS		128.0		125.5	128.0	5.23	5.33	01/08/99	05:30 AM	01/08/99	08:00 AM
0.0	0.0	0.0 HRS		128.0		128.0	128.0	5.33	5.33	01/08/99	08:00 AM	01/08/99	08:01 AM
0.0	0.0	0.0 HRS			128.0	128.0	128.0	5.33	5.33	01/08/99	08:01 AM	01/08/99	08:01 AM
0.0	0.0	0.0 HRS			128.0	128.0	128.0	5.33	5.33	01/08/99	08:01 AM	01/08/99	08:01 AM
0.0	0.0	0.0 HRS			128.0	128.0	128.0	5.33	5.33	01/08/99	08:01 AM	01/08/99	08:01 AM
2.5		2.5 HRS		128.0			128.0			01/08/99	05:30 AM	01/08/99	08:01 AM
										HRS/CY	2.5		
										OK			
0.0	0.0	0.0 HRS	125.5			125.5	125.5	5.23	5.23	01/08/99	05:30 AM	01/08/99	05:30 AM
2.50	0.0	2.5 HRS		128.0		125.5	128.0	5.23	5.33	01/08/99	05:30 AM	01/08/99	08:01 AM
0.0	0.0	0.0 HRS		128.0		128.0	128.0	5.33	5.33	01/08/99	08:01 AM	01/08/99	08:01 AM
0.0	0.0	0.0 HRS			128.0	128.0	128.0	5.33	5.33	01/08/99	08:01 AM	01/08/99	08:01 AM
0.0	0.0	0.0 HRS			128.0	128.0	128.0	5.33	5.33	01/08/99	08:01 AM	01/08/99	08:01 AM
0.0	0.0	0.0 HRS			128.0	128.0	128.0	5.33	5.33	01/08/99	08:01 AM	01/08/99	08:01 AM
2.5		2.5 HRS		128.0			128.0			01/08/99	05:30 AM	01/08/99	08:01 AM
										HRS/CY	2.5		
										OK			

FIG.23C-2

	FIRST SHIFT				SECOND SHIFT			
	START	07:00 AM	FINISH	03:00 PM	START	03:00 PM	FINISH	11:00 PM
OPERATION	DATE	TIME	DATE	TIME	DATE	TIME	DATE	TIME
1.1.1.1 176 MULTI-STAGE POOL	01/08/99	08:00 AM	01/08/99	08:00 AM				
SET UP	01/08/99	08:00 AM	01/08/99	08:00 AM				
INPUT 1								
INPUT 2								
INPUT 3								
INPUT 4								
INPUT 5								
INPUT 6								
POOL INPUTS	01/08/99	08:00 AM	01/08/99	08:00 AM				
SUB TOTAL								
2.1.1.1 51 OUTLET HEAT EXCHANGE								
SET UP			01/08/99	08:00 AM				
TRANSFER	01/08/99	08:00 AM	01/08/99	10:30 AM				
WASH	01/08/99	10:30 AM	01/08/99	11:07 AM				
CIP	01/08/99	11:07 AM	01/08/99	11:07 AM				
SIP	01/08/99	11:07 AM	01/08/99	11:07 AM				
CLEAN UP	01/08/99	11:07 AM	01/08/99	01:07 PM				
SUB TOTAL								
3.1.1.1 26 CONT. CERT/SOLIDS								
SET UP	01/08/99	09:30 AM	01/08/99	10:30 AM			01/08/99	04:30 PM
CENTRIFUGATION	01/08/99	10:30 AM			01/08/99	04:30 PM	01/08/99	04:30 PM
WASH					01/08/99	04:30 PM	01/08/99	04:30 PM
CIP					01/08/99	04:30 PM	01/08/99	04:30 PM
SIP					01/08/99	04:30 PM	01/08/99	04:30 PM
CLEAN UP					01/08/99	04:30 PM	01/08/99	04:30 PM
SUB TOTAL								
4.1.1.1 48 RESOLUBILIZATION								
SET UP					01/08/99	03:30 PM	01/08/99	04:30 PM
DILUTION					01/08/99	04:30 PM	01/08/99	07:30 PM
MO					01/08/99	07:30 PM	01/08/99	07:30 PM
CIP					01/08/99	07:30 PM	01/08/99	07:30 PM
SIP					01/08/99	07:30 PM	01/08/99	07:30 PM
CLEAN UP					01/08/99	07:30 PM	01/08/99	08:30 PM
SUB TOTAL								
5.1.1.1 61 INLET HEAT EXCHANGE								
SET UP					01/08/99	06:30 PM	01/08/99	07:30 PM
TRANSFER					01/08/99	07:30 PM	01/08/99	10:00 PM
WASH					01/08/99	10:00 PM	01/08/99	10:00 PM

FIG.23D-1

THIRD SHIFT			
START	11:04 PM	FINISH	04:07 AM
DATE	TIME	DATE	TIME
01/08/99	07:00 AM		

FIG.23D-2

	FIRST SHIFT				SECOND SHIFT			
	START	07:00 AM	FINISH	03:00 PM	START	01:00 PM	FINISH	11:00 PM
OPERATION	DATE	TIME	DATE	TIME	DATE	TIME	DATE	TIME
CIP					01/08/99	10:00 PM	01/08/99	10:00 PM
SIP					01/08/99	10:00 PM	01/08/99	10:00 PM
CLEAN UP					01/08/99	10:00 PM	01/08/99	10:00 PM
SUB TOTAL								
6.1.1.1 31 HOMOGENIZATION								
SET UP					01/08/99	09:00 PM	01/08/99	10:00 PM
LYCIS					01/08/99	10:00 PM		
WASH								
CIP								
SIP								
CLEAN UP								
SUB TOTAL								
7.1.1.1 51 OUTLET HEAT EXCHANGE								
SET UP								
TRANSFER								
WASH								
CIP								
SIP								
CLEAN UP								
SUB TOTAL								
5.1.2.1 61 INLET HEAT EXCHANGE								
SET UP								
TRANSFER								
WASH								
CIP								
SIP								
CLEAN UP								
SUB TOTAL								
6.1.2.1 31 HOMOGENIZATION								
SET UP								
LYCIS								
WASH								
CIP								
SIP								
CLEAN UP								
SUB TOTAL								
7.1.2.1 51 OUTLET HEAT EXCHANGE								

FIG.23E-1

THIRD SHIFT			
START	11:00 PM	FINISH	08:00 AM
DATE	TIME	DATE	TIME
		01/08/99	12:30 AM
01/08/99	12:30 AM	01/08/99	12:30 AM
01/08/99	12:30 AM	01/08/99	12:30 AM
01/08/99	11:30 PM	01/08/99	12:30 AM
01/08/99	12:30 AM	01/08/99	03:00 AM
01/08/99	03:00 AM	01/08/99	03:00 AM
01/08/99	03:00 AM	01/08/99	03:00 AM
01/08/99	03:00 AM	01/08/99	03:00 AM
01/08/99	03:00 AM	01/08/99	03:00 AM
01/08/99	03:00 AM	01/08/99	03:00 AM
01/08/99	03:00 AM	01/08/99	05:30 AM
01/08/99	05:30 AM	01/08/99	05:30 AM
01/08/99	05:30 AM	01/08/99	05:30 AM
01/08/99	05:30 AM	01/08/99	05:30 AM
01/08/99	05:30 AM	01/08/99	05:30 AM
01/08/99	03:00 AM	01/08/99	03:00 AM
01/08/99	03:00 AM	01/08/99	05:30 AM
01/08/99	05:30 AM	01/08/99	05:30 AM
01/08/99	05:30 AM	01/08/99	05:30 AM
01/08/99	05:30 AM	01/08/99	05:30 AM
01/08/99	05:30 AM	01/08/99	05:30 AM

FIG.23E-2

	FIRST SHIFT				SECOND SHIFT			
	START	07:00 AM	FINISH	03:00 PM	START	03:00 PM	FINISH	11:00 PM
OPERATION	DATE	TIME	DATE	TIME	DATE	TIME	DATE	TIME
SET UP								
TRANSFER								
WASH								
CIP								
SIP								
CLEAN UP								
SUB TOTAL								
5.1.3.1 61 INLET HEAT EXCHANGE								
SET UP								
TRANSFER			01/08/99	08:00 AM				
WASH	01/08/99	08:00 AM	01/08/99	08:01 AM				
CIP	01/08/99	08:01 AM	01/08/99	08:01 AM				
SIP	01/08/99	08:01 AM	01/08/99	08:01 AM				
CLEAN UP	01/08/99	08:01 AM	01/08/99	08:01 AM				
SUB TOTAL								
6.1.3.1 31 HOMMOGENIZATION								
SET UP								
LYCIS			01/08/99	08:00 AM				
WASH	01/08/99	08:00 AM	01/08/99	08:01 AM				
CIP	01/08/99	08:01 AM	01/08/99	08:01 AM				
SIP	01/08/99	08:01 AM	01/08/99	08:01 AM				
CLEAN UP	01/08/99	08:01 AM	01/08/99	08:01 AM				
SUB TOTAL								
7.1.3.1 51 OUTLET HEAT EXCHANGE								
SET UP								
TRANSFER			01/08/99	08:01 AM				
WASH	01/08/99	08:01 AM	01/08/99	08:01 AM				
CIP	01/08/99	08:01 AM	01/08/99	08:01 AM				
SIP	01/08/99	08:01 AM	01/08/99	08:01 AM				
CLEAN UP	01/08/99	08:01 AM	01/08/99	08:01 AM				
SUB TOTAL								

FIG.23F-1

THIRD SHIFT			
START	11:00 PM	FINISH	05:30 AM
DATE	TIME	DATE	TIME
01/08/99 01/08/99 01/08/99 01/08/99 01/08/99 01/08/99	03:00 AM 03:00 AM 05:30 AM 05:30 AM 05:30 AM 05:30 AM	01/08/99 01/08/99 01/08/99 01/08/99 01/08/99 01/08/99	03:00 AM 05:30 AM 05:30 AM 05:30 AM 05:30 AM 05:30 AM
01/08/99 01/08/99	05:30 AM 05:30 AM	01/08/99	05:30 AM
01/08/99 01/08/99	05:30 AM 05:30 AM	01/08/99	05:30 AM
01/08/99 01/08/99	05:30 AM 05:30 AM	01/08/99	05:30 AM

FIG.23F-2

FIG. 24

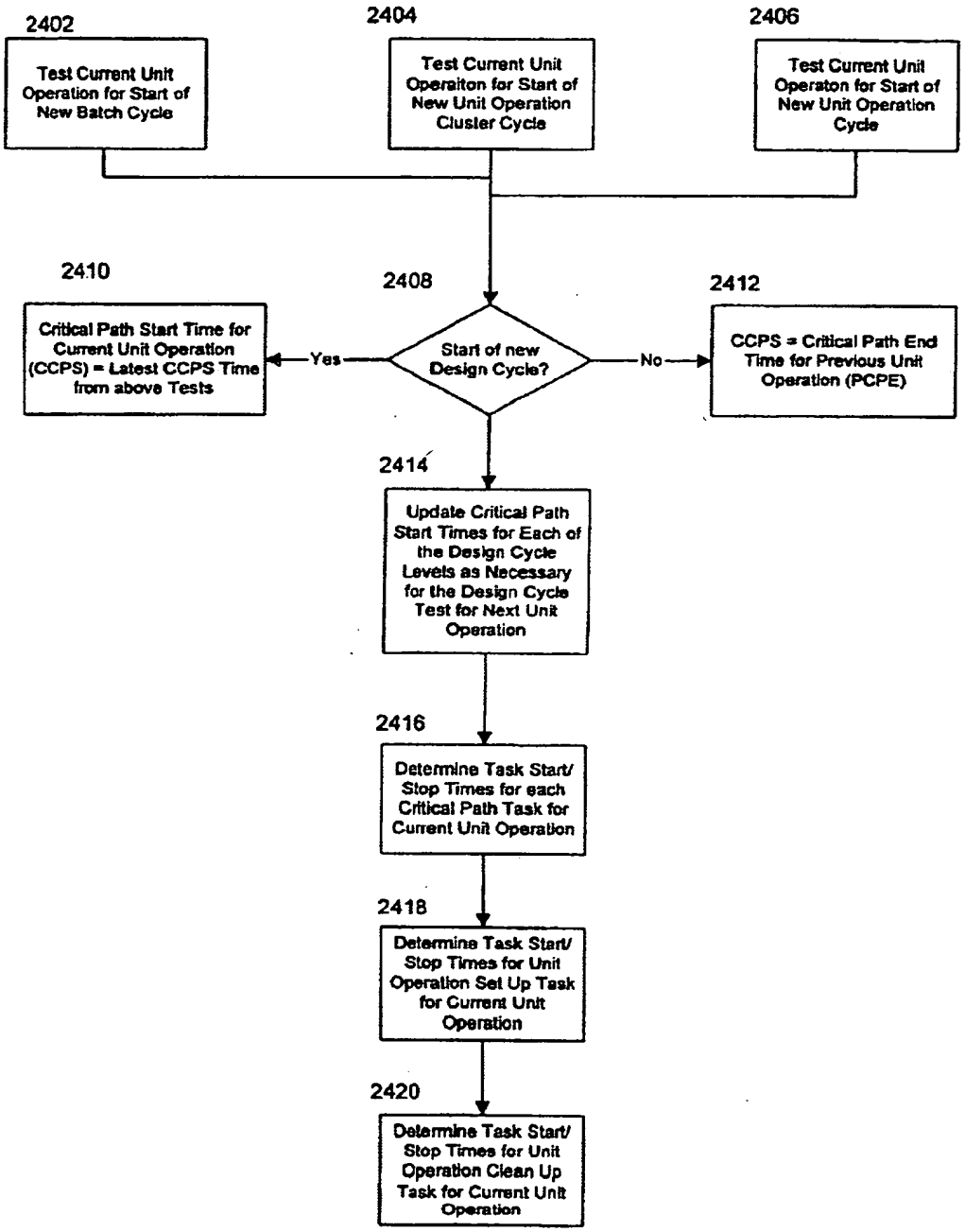

2402
Test Current Unit Operation for Start of New Batch Cycle
2404
Test Current Unit Operaiton for Start of New Unit Operation Cluster Cycle
2406
Test Current Unit Operaton for Start of New Unit Operation Cycle
2410
Critical Path Start Time for Current Unit Operation (CCPS) = Latest CCPS Time from above Tests
Yes
2408
Start of new Design Cycle?
No
2412
CCPS = Critical Path End Time for Previous Unit Operation (PCPE)
2414
Update Critical Path Start Times for Each of the Design Cycle Levels as Necessary for the Design Cycle Test for Next Unit Operation
2416
Determine Task Start/ Stop Times for each Critical Path Task for Current Unit Operation
2418
Determine Task Start/ Stop Times for Unit Operation Set Up Task for Current Unit Operation
2420
Determine Task Start/ Stop Times for Unit Operation Clean Up Task for Current Unit Operation

FIG. 25

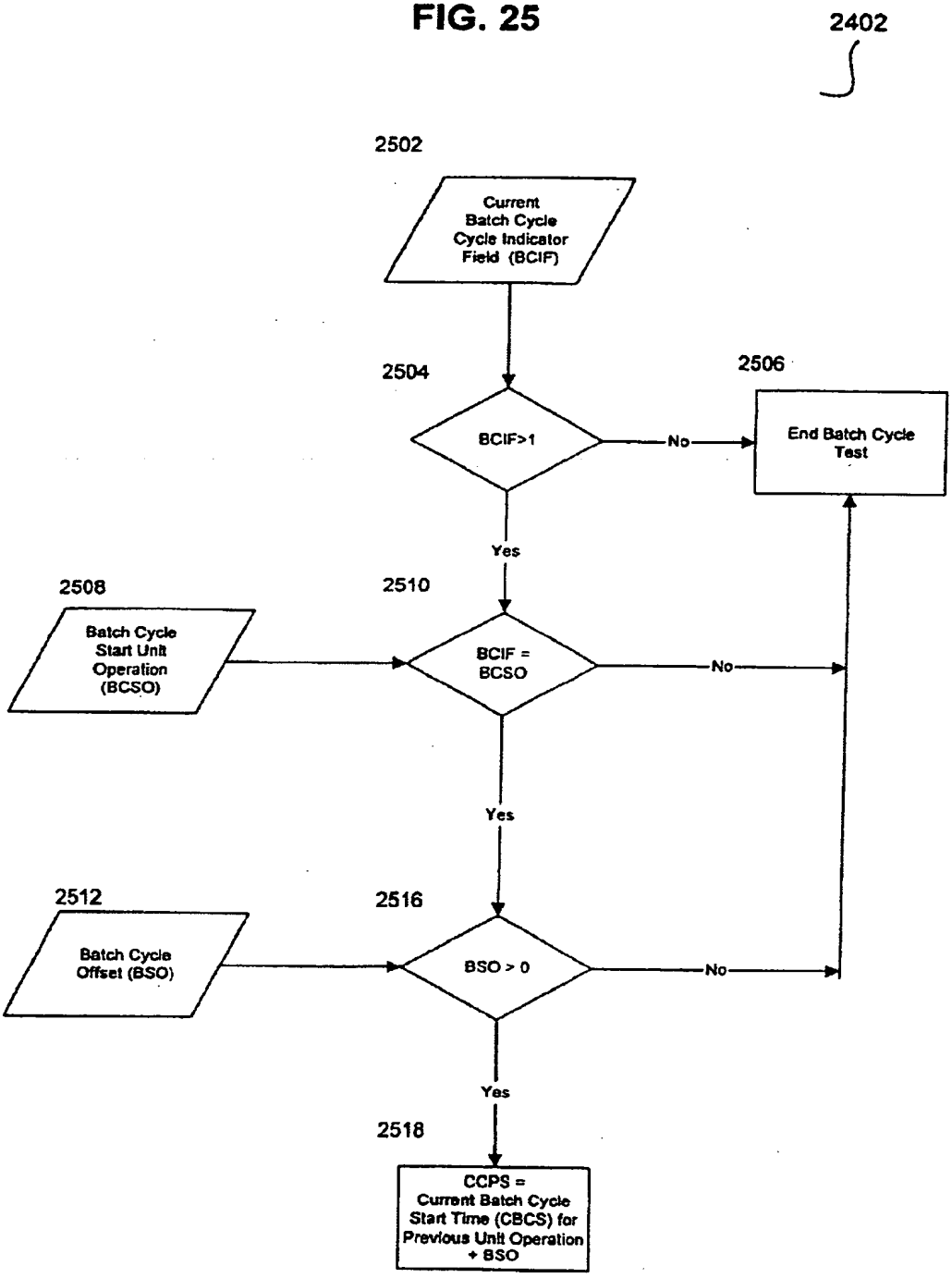

2402
2502
Current Batch Cycle Cycle Indicator Field (BCIF)
2504
BCIF>1
No
2506
End Batch Cycle Test
Yes
2508
Batch Cycle Start Unit Operation (BCSO)
2510
BCIF = BCSO
No
Yes
2512
Batch Cycle Offset (BSO)
2516
BSO > 0
No
Yes
2518
CCPS = Current Batch Cycle Start Time (CBCS) for Previous Unit Operation + BSO

FIG. 26

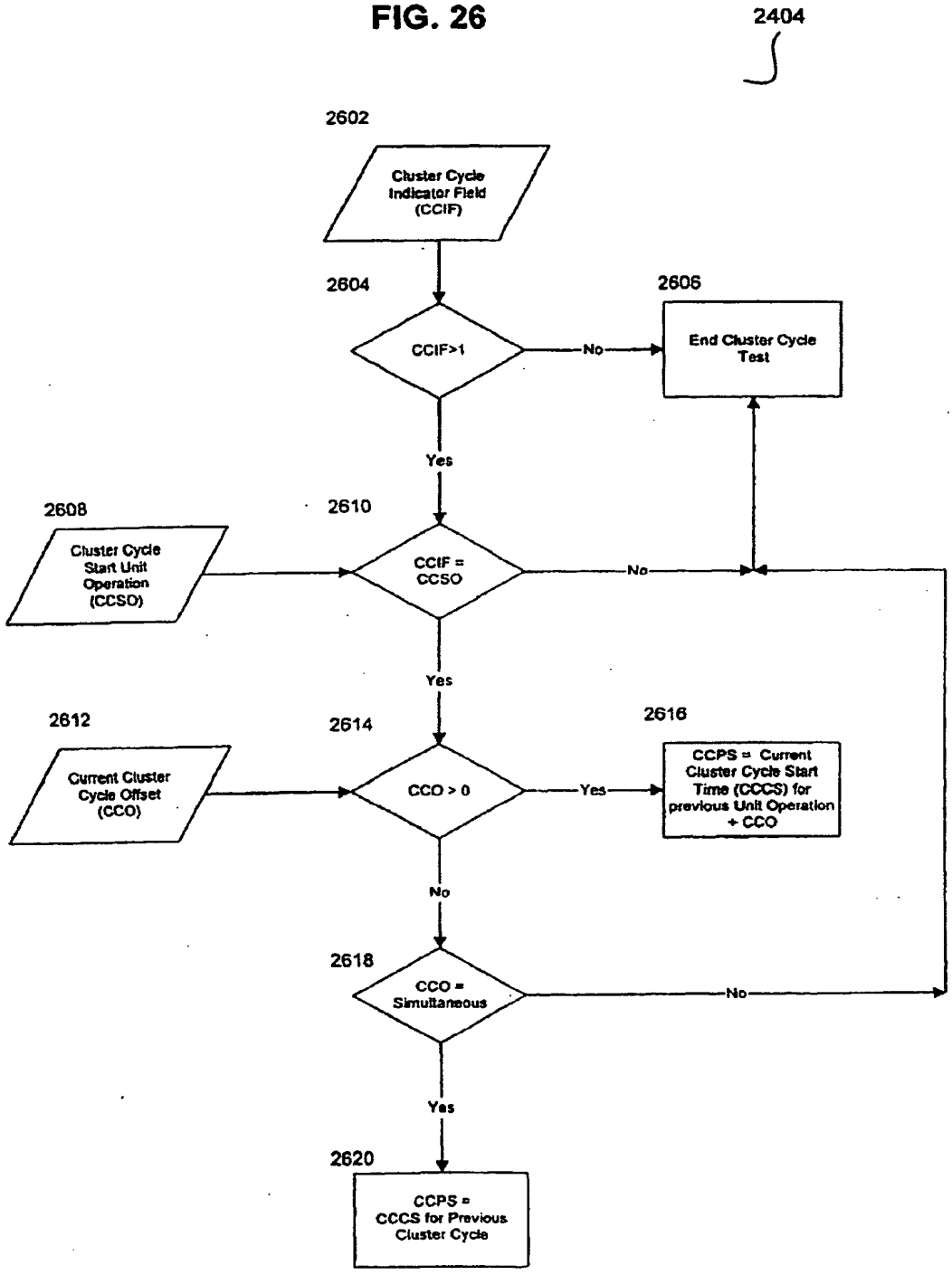

2404
2602
Cluster Cycle Indicator Field (CCIF)
2604
CCIF>1
No
2606
End Cluster Cycle Test
Yes
2608
Cluster Cycle Start Unit Operation (CCSO)
2610
CCIF = CCSO
No
Yes
2612
Current Cluster Cycle Offset (CCO)
2614
CCO > 0
Yes
2616
CCPS = Current Cluster Cycle Start Time (CCCS) for previous Unit Operation + CCO
No
2618
CCO = Simultaneous
No
Yes
2620
CCPS = CCCS for Previous Cluster Cycle

FIG. 27

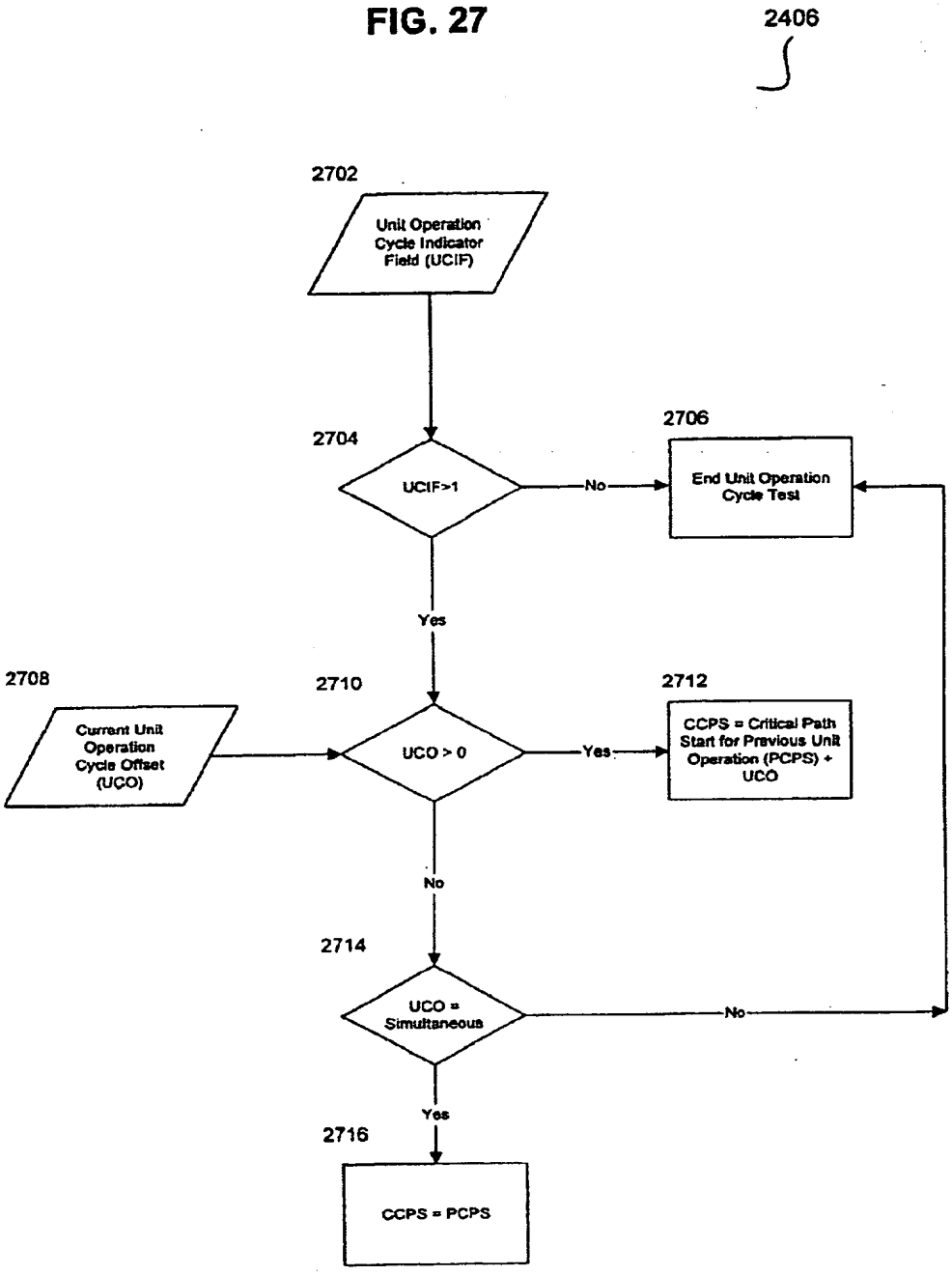

2406
2702
Unit Operation Cycle Indicator Field (UCIF)
2704
UCIF>1
No
2706
End Unit Operation Cycle Test
Yes
2708
Current Unit Operation Cycle Offset (UCO)
2710
UCO > 0
Yes
2712
CCPS = Critical Path Start for Previous Unit Operation (PCPS) + UCO
No
2714
UCO = Simultaneous
No
Yes
2716
CCPS = PCPS

FIG. 28

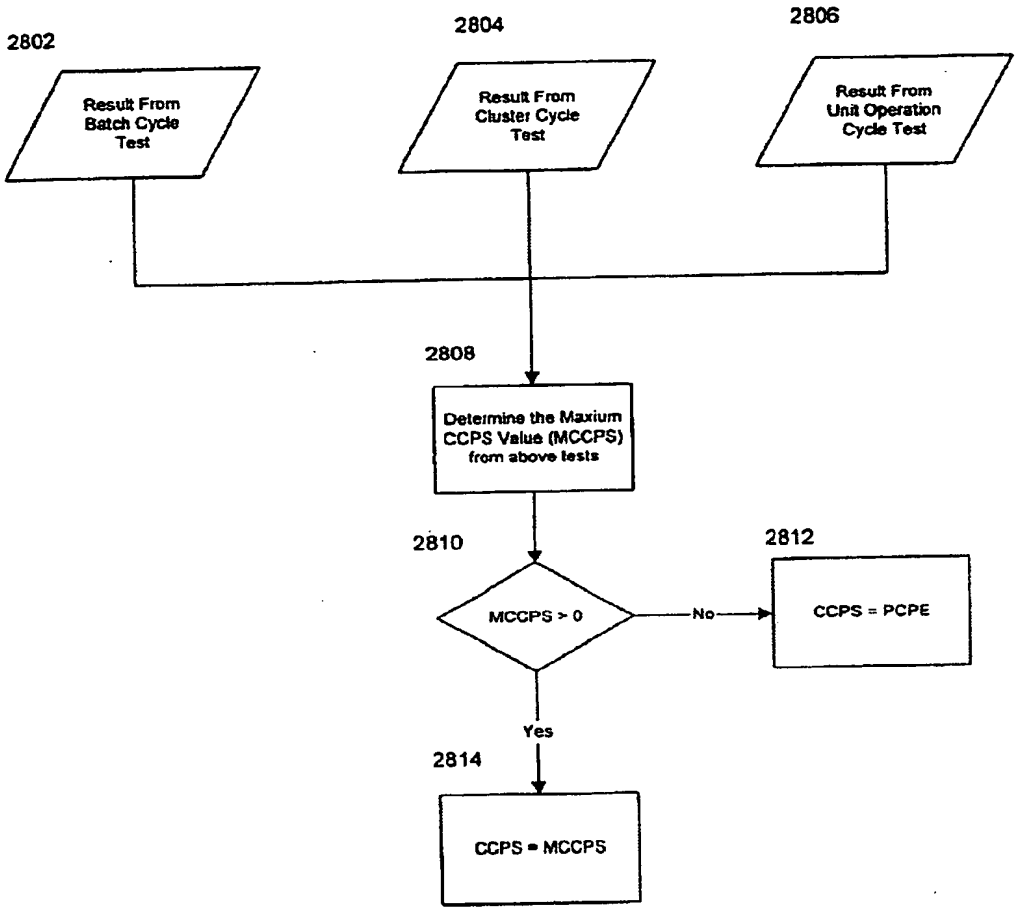

2802
Result From Batch Cycle Test
2804
Result From Cluster Cycle Test
2806
Result From Unit Operation Cycle Test
2808
Determine the Maxium CCPS Value (MCCPS) from above tests
2810
MCCPS > 0
No
2812
CCPS = PCPE
Yes
2814
CCPS = MCCPS

FIG. 29

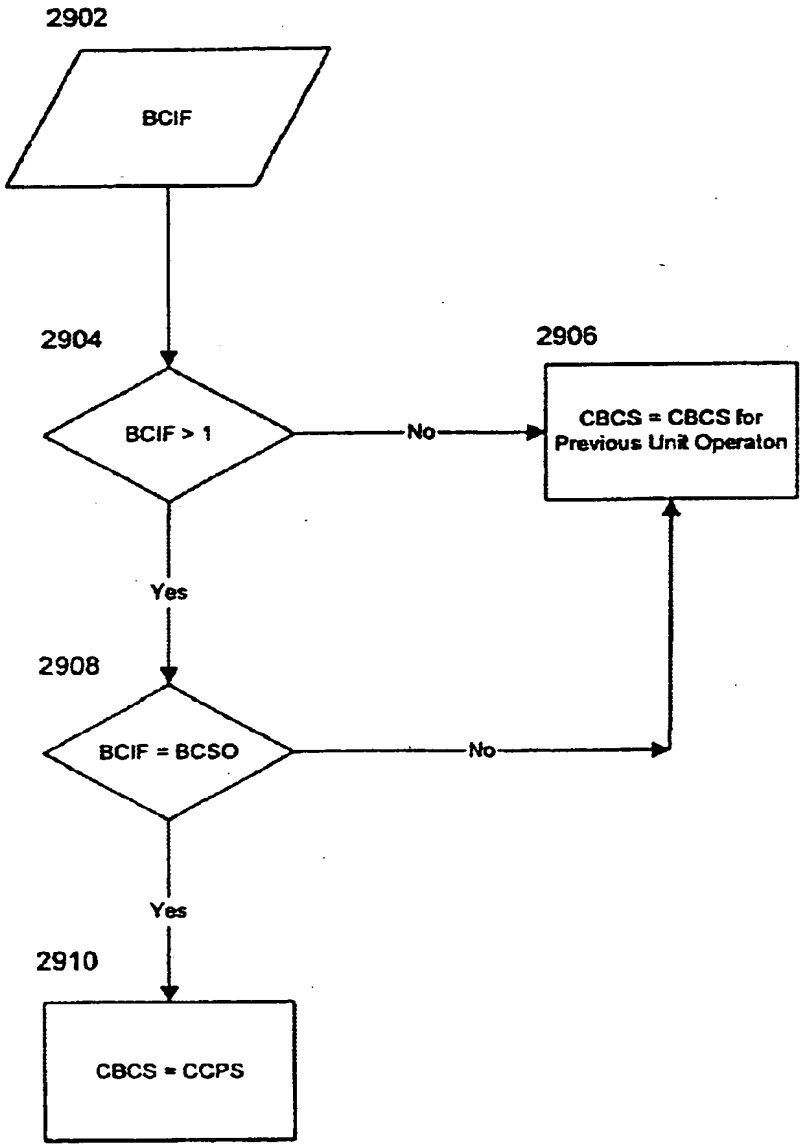

2902
BCIF
2904
BCIF > 1
No
2906
CBCS = CBCS for Previous Unit Operaton
Yes
2908
BCIF = BCSO
No
Yes
2910
CBCS = CCPS

FIG. 30

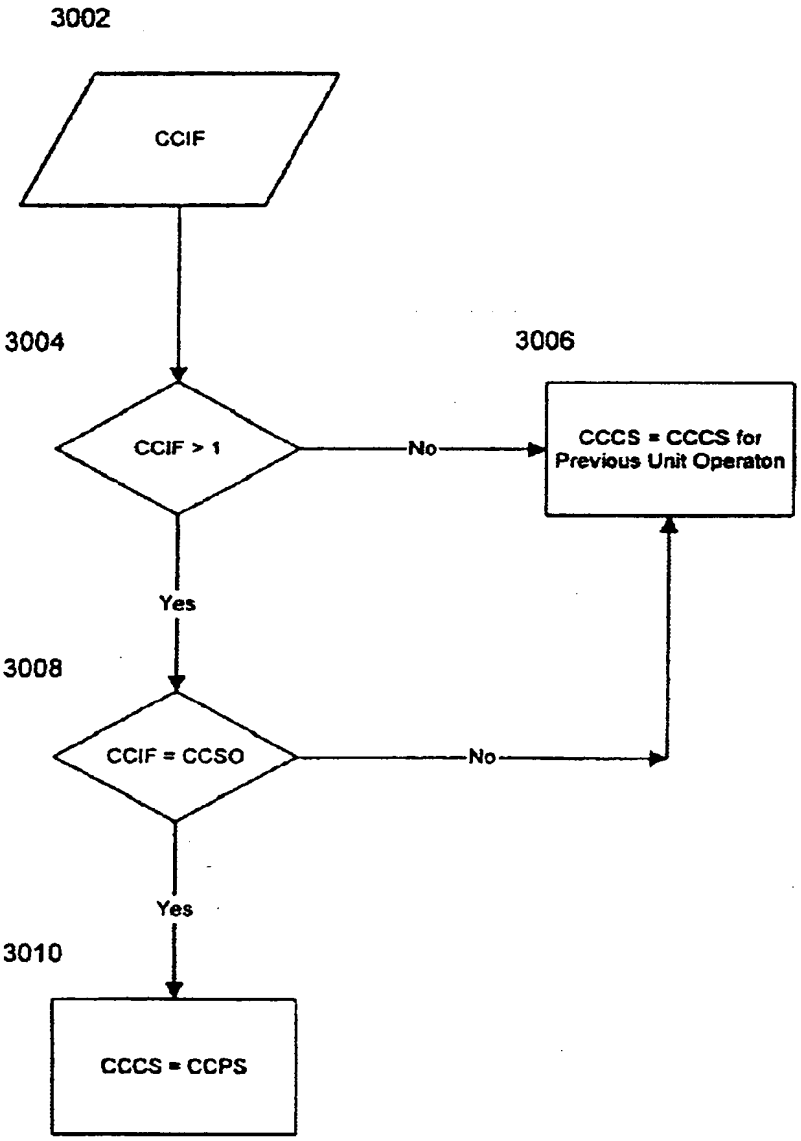

3002
CCIF
3004
CCIF > 1
No
3006
CCCS = CCCS for Previous Unit Operaton
Yes
3008
CCIF = CCSO
No
Yes
3010
CCCS = CCPS

FIG. 31

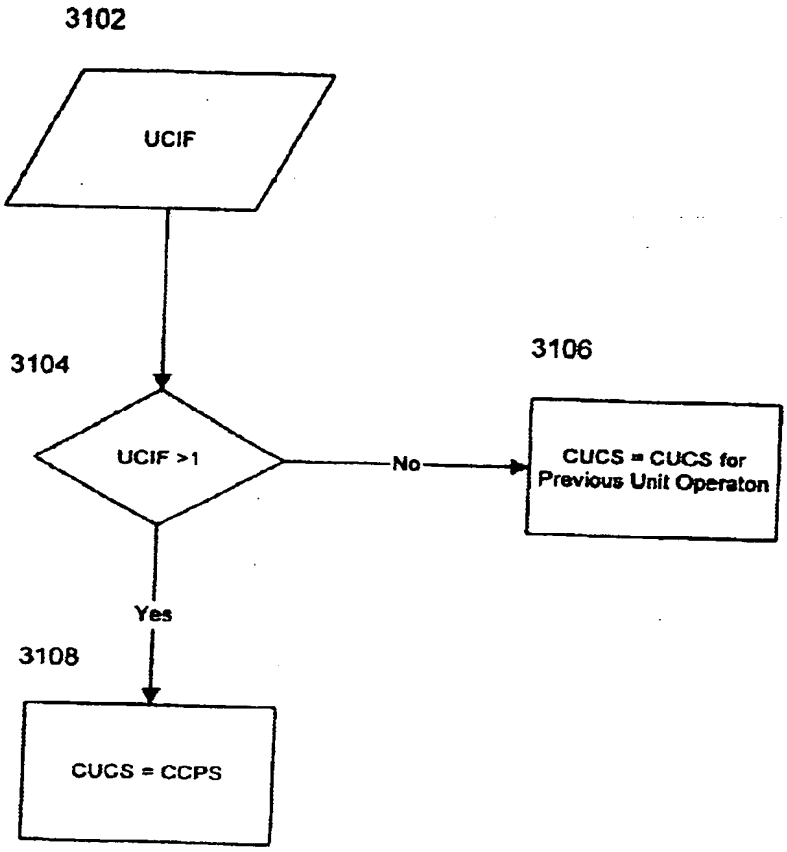

3102
UCIF
3104
UCIF >1
No
3106
CUCS = CUCS for Previous Unit Operaton
Yes
3108
CUCS = CCPS

FIG. 32

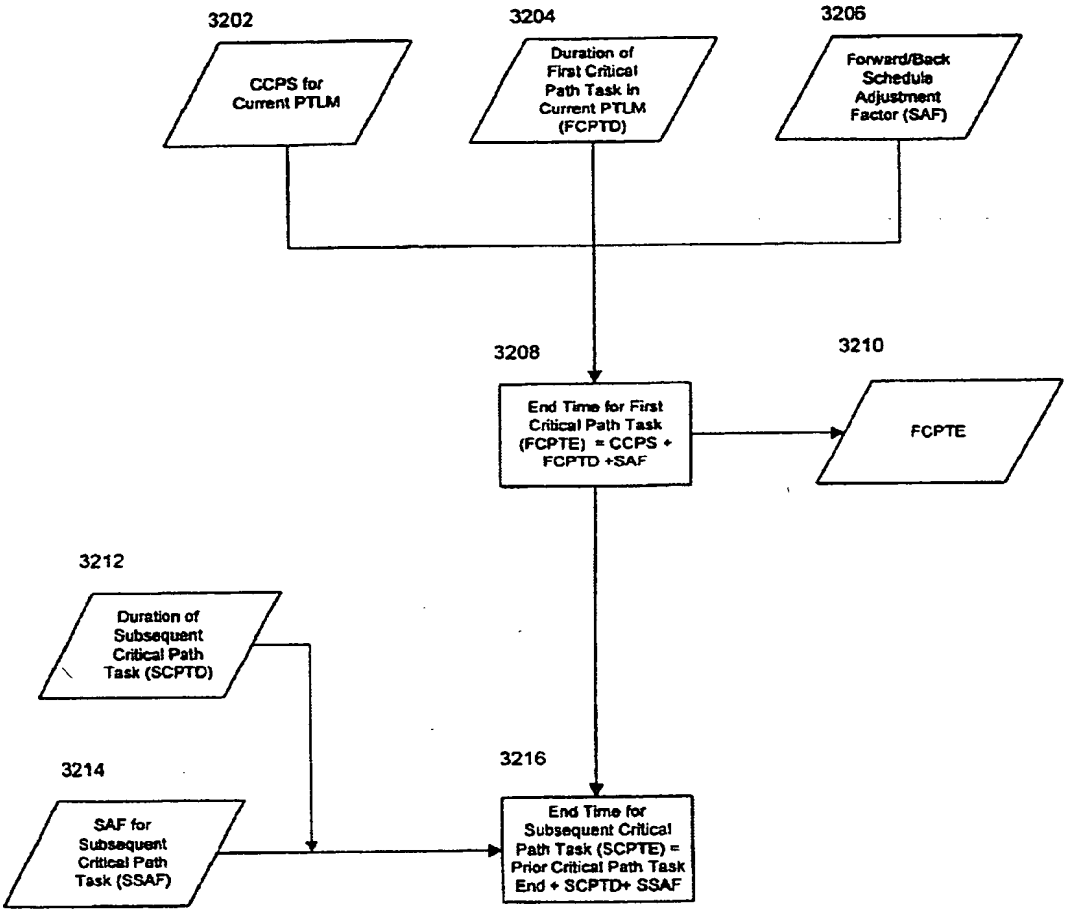

3202
CCPS for Current PTLM
3204
Duration of First Critical Path Task in Current PTLM (FCPTD)
3206
Forward/Back Schedule Adjustment Factor (SAF)
3208
End Time for First Critical Path Task (FCPTE) = CCPS + FCPTD +SAF
3210
FCPTE
3212
Duration of Subsequent Critical Path Task (SCPTD)
3214
SAF for Subsequent Critical Path Task (SSAF)
3216
End Time for Subsequent Critical Path Task (SCPTE) = Prior Critical Path Task End + SCPTD+ SSAF

FIG. 33

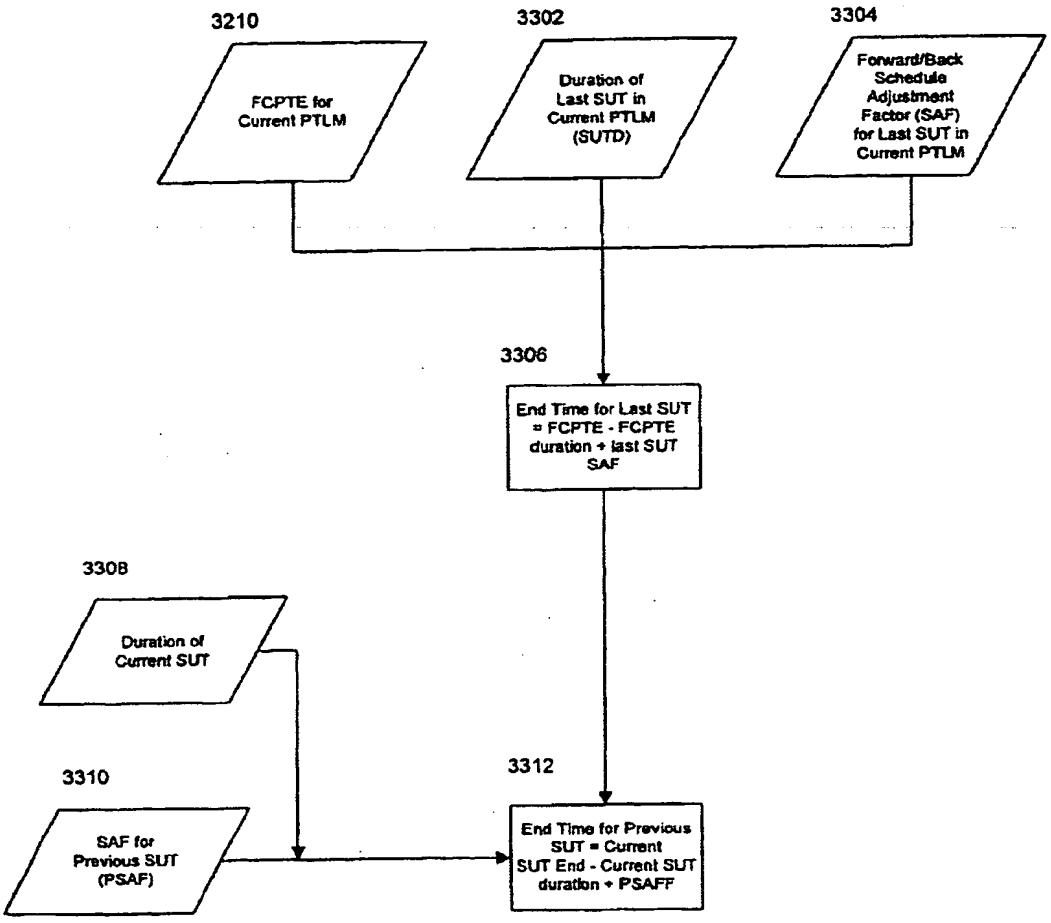
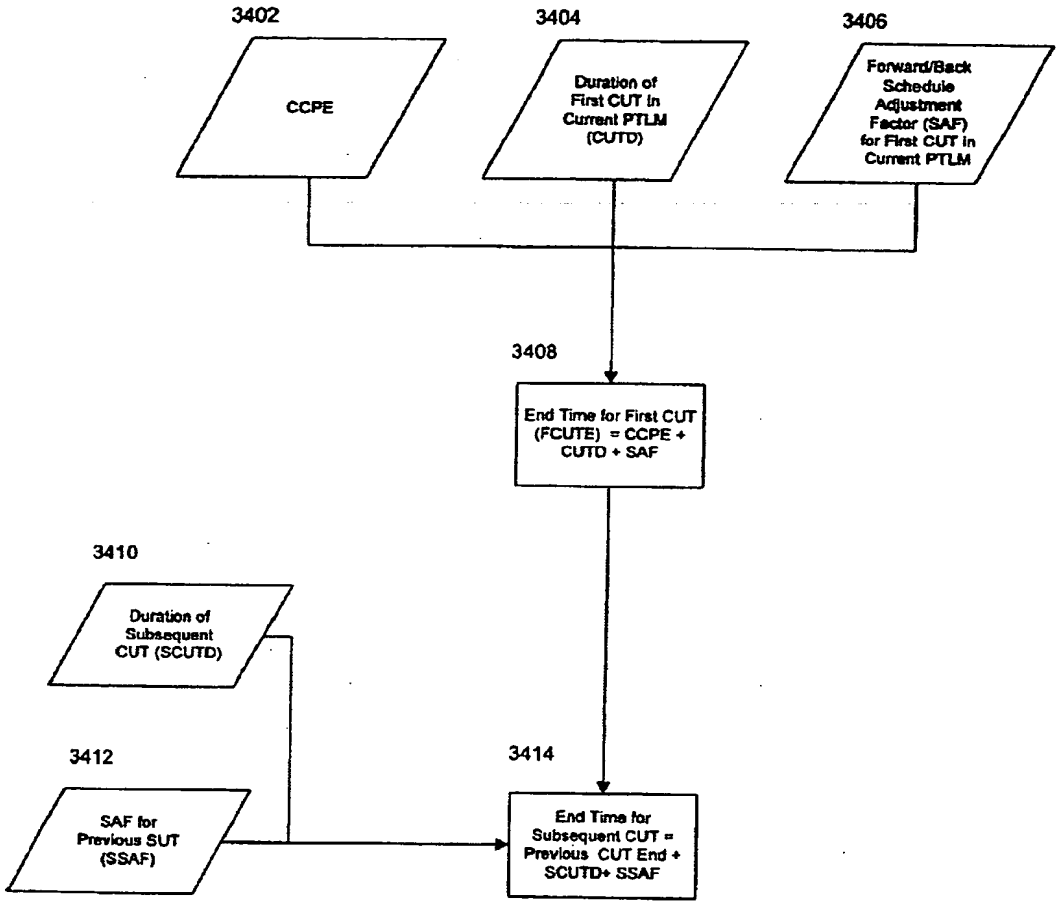

3210
FCPTE for Current PTLM
3302
Duration of Last SUT in Current PTLM (SUTD)
3304
Forward/Back Schedule Adjustment Factor (SAF) for Last SUT in Current PTLM
3306
End Time for Last SUT = FCPTE - FCPTE duration + last SUT SAF
3308
Duration of Current SUT
3310
SAF for Previous SUT (PSAF)
3312
End Time for Previous SUT = Current SUT End - Current SUT duration + PSAFF

FIG. 34


3402
CCPE
3404
Duration of First CUT in Current PTLM (CUTD)
3406
Forward/Back Schedule Adjustment Factor (SAF) for First CUT in Current PTLM
3408
End Time for First CUT (FCUTE) = CCPE + CUTD + SAF
3410
Duration of Subsequent CUT (SCUTD)
3412
SAF for Previous SUT (SSAF)
3414
End Time for Subsequent CUT = Previous CUT End + SCUTD+ SSAF

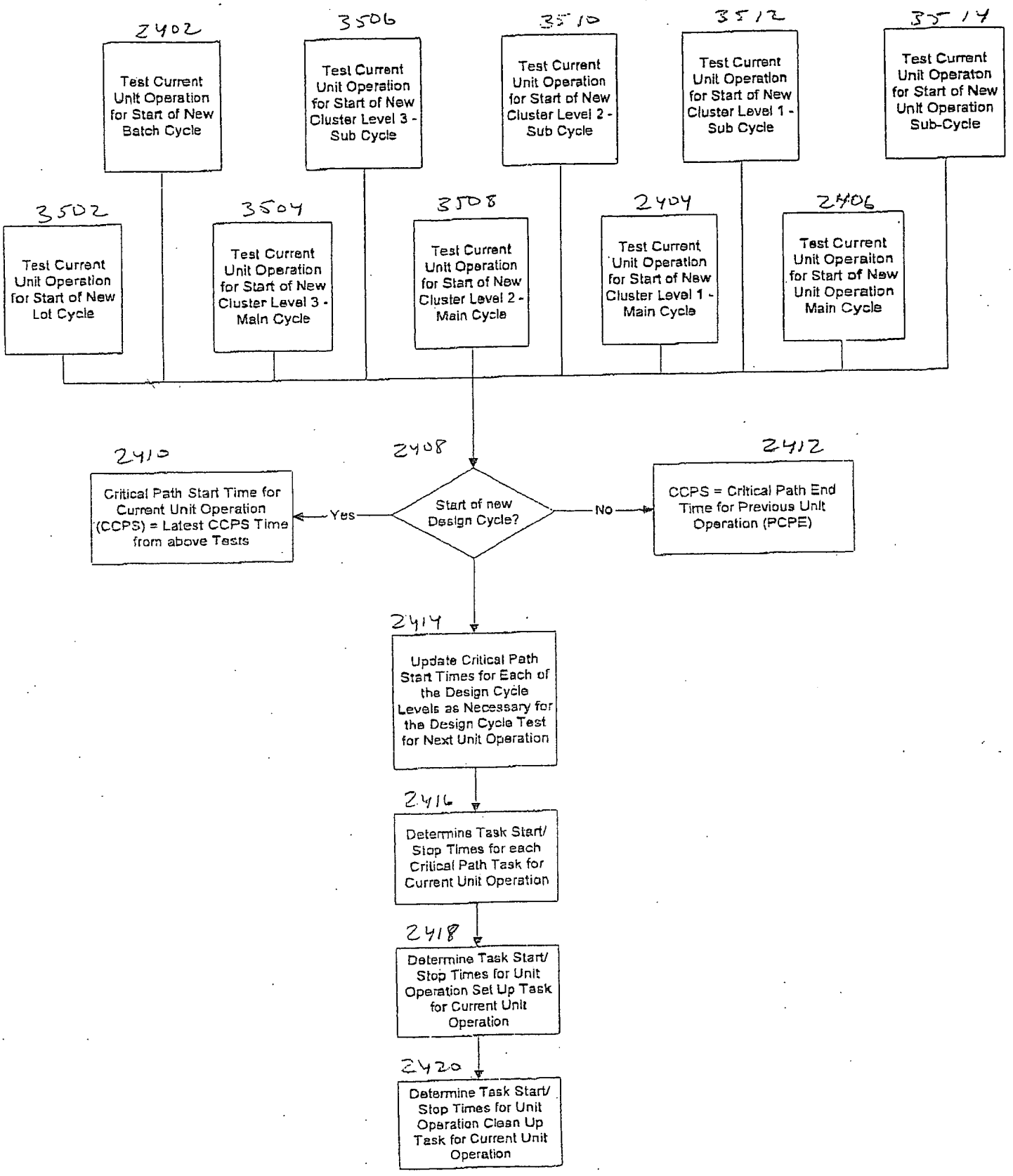

2402
Test Current Unit Operation for Start of New Batch Cycle
3506
Test Current Unit Operation for Start of New Cluster Level 3 - Sub Cycle
3510
Test Current Unit Operation for Start of New Cluster Level 2 - Sub Cycle
3512
Test Current Unit Operation for Start of New Cluster Level 1 - Sub Cycle
3514
Test Current Unit Operaton for Start of New Unit Operation Sub-Cycle
3502
Test Current Unit Operation for Start of New Lot Cycle
3504
Test Current Unit Operation for Start of New Cluster Level 3 - Main Cycle
3508
Test Current Unit Operation for Start of New Cluster Level 2 - Main Cycle
2404
Test Current Unit Operation for Start of New Cluster Level 1 - Main Cycle
2406
Test Current Unit Operaiton for Start of New Unit Operation Main Cycle
2410
Critical Path Start Time for Current Unit Operation (CCPS) = Latest CCPS Time from above Tests
Yes
2408
Start of new Design Cycle?
No
2412
CCPS = Critical Path End Time for Previous Unit Operation (PCPE)
2414
Update Critical Path Start Times for Each of the Design Cycle Levels as Necessary for the Design Cycle Test for Next Unit Operation
2416
Determine Task Start/ Stop Times for each Critical Path Task for Current Unit Operation
2418
Determine Task Start/ Stop Times for Unit Operation Set Up Task for Current Unit Operation
2420
Determine Task Start/ Stop Times for Unit Operation Clean Up Task for Current Unit Operation

FIG. 35

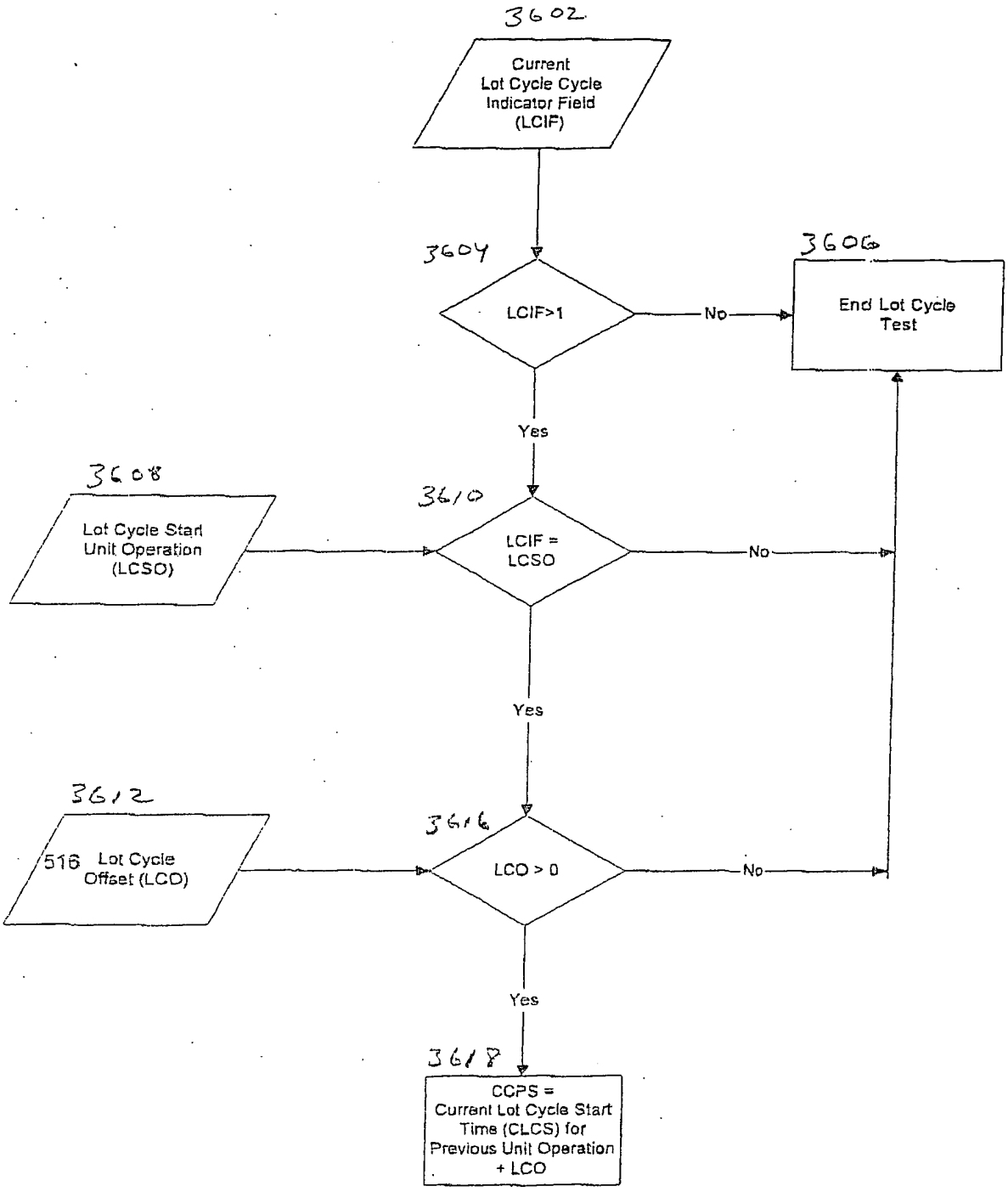

3602
Current Lot Cycle Cycle Indicator Field (LCIF)
3604
LCIF>1
No
3606
End Lot Cycle Test
Yes
3608
Lot Cycle Start Unit Operation (LCSO)
3610
LCIF = LCSO
No
Yes
3612
516 Lot Cycle Offset (LCO)
3616
LCO > 0
No
Yes
3618
CCPS = Current Lot Cycle Start Time (CLCS) for Previous Unit Operation + LCO

FIG. 36

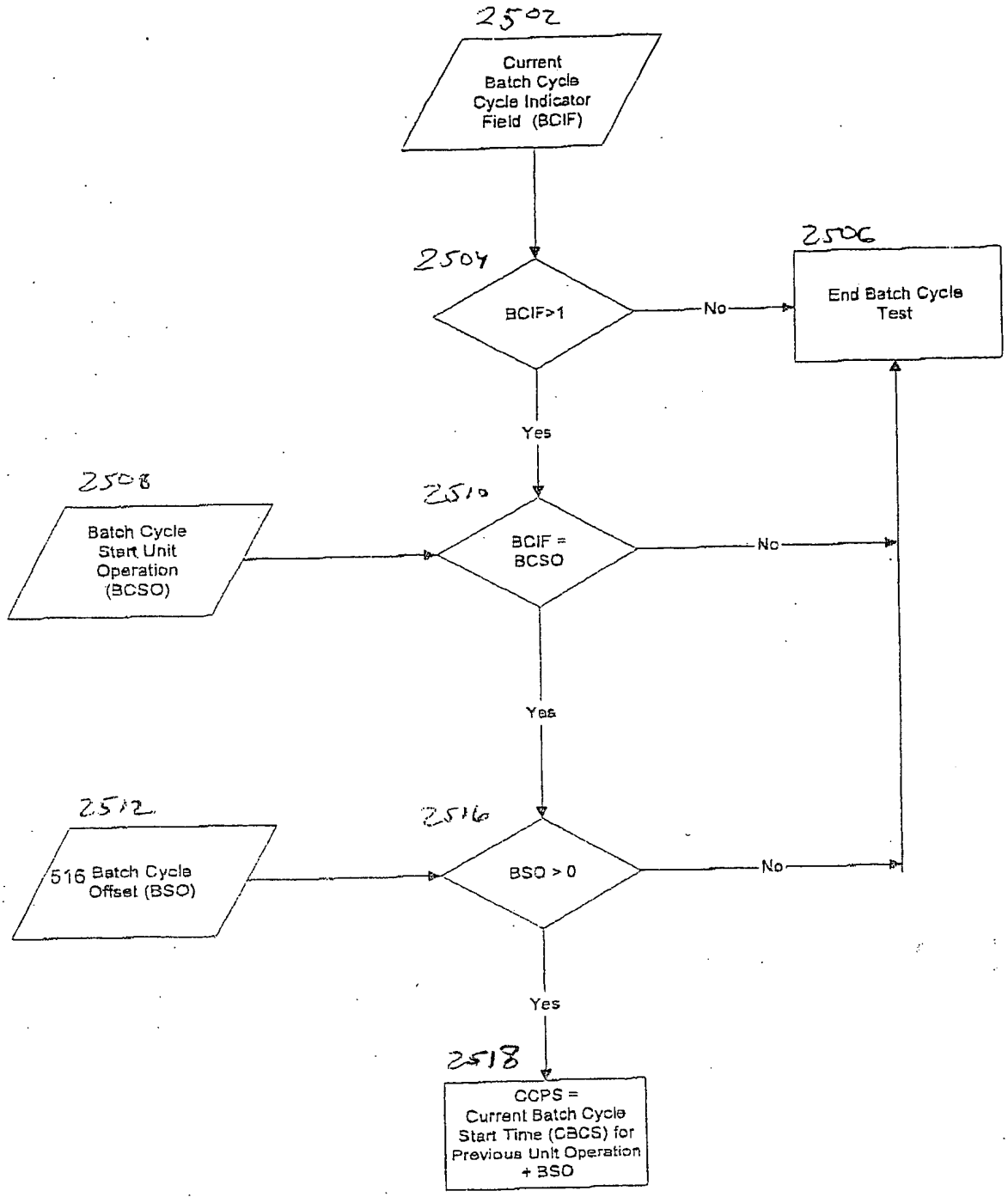

2502
Current Batch Cycle Cycle Indicator Field (BCIF)
2504
BCIF>1
No
2506
End Batch Cycle Test
Yes
2508
Batch Cycle Start Unit Operation (BCSO)
2510
BCIF = BCSO
No
Yes
2512
516 Batch Cycle Offset (BSO)
2516
BSO > 0
No
Yes
2518
CCPS = Current Batch Cycle Start Time (CBCS) for Previous Unit Operation + BSO

FIG 37

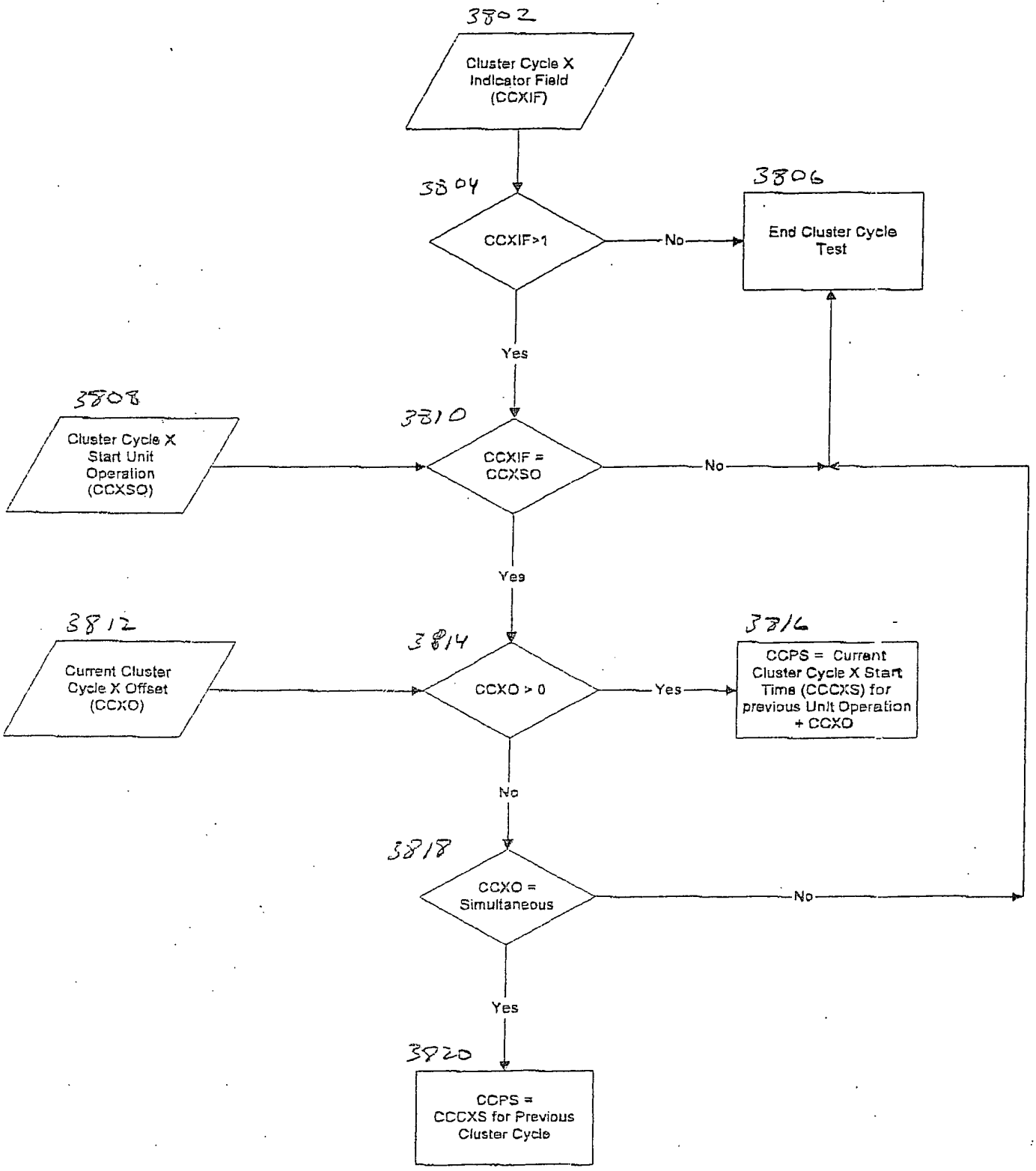

3802
Cluster Cycle X Indicator Field (CCXIF)
3804
CCXIF>1
No
3806
End Cluster Cycle Test
Yes
3808
Cluster Cycle X Start Unit Operation (CCXSO)
3810
CCXIF = CCXSO
No
Yes
3812
Current Cluster Cycle X Offset (CCXO)
3814
CCXO > 0
Yes
3816
CCPS = Current Cluster Cycle X Start Time (CCCXS) for previous Unit Operation + CCXO
No
3818
CCXO = Simultaneous
No
Yes
3820
CCPS = CCCXS for Previous Cluster Cycle

FIG 38

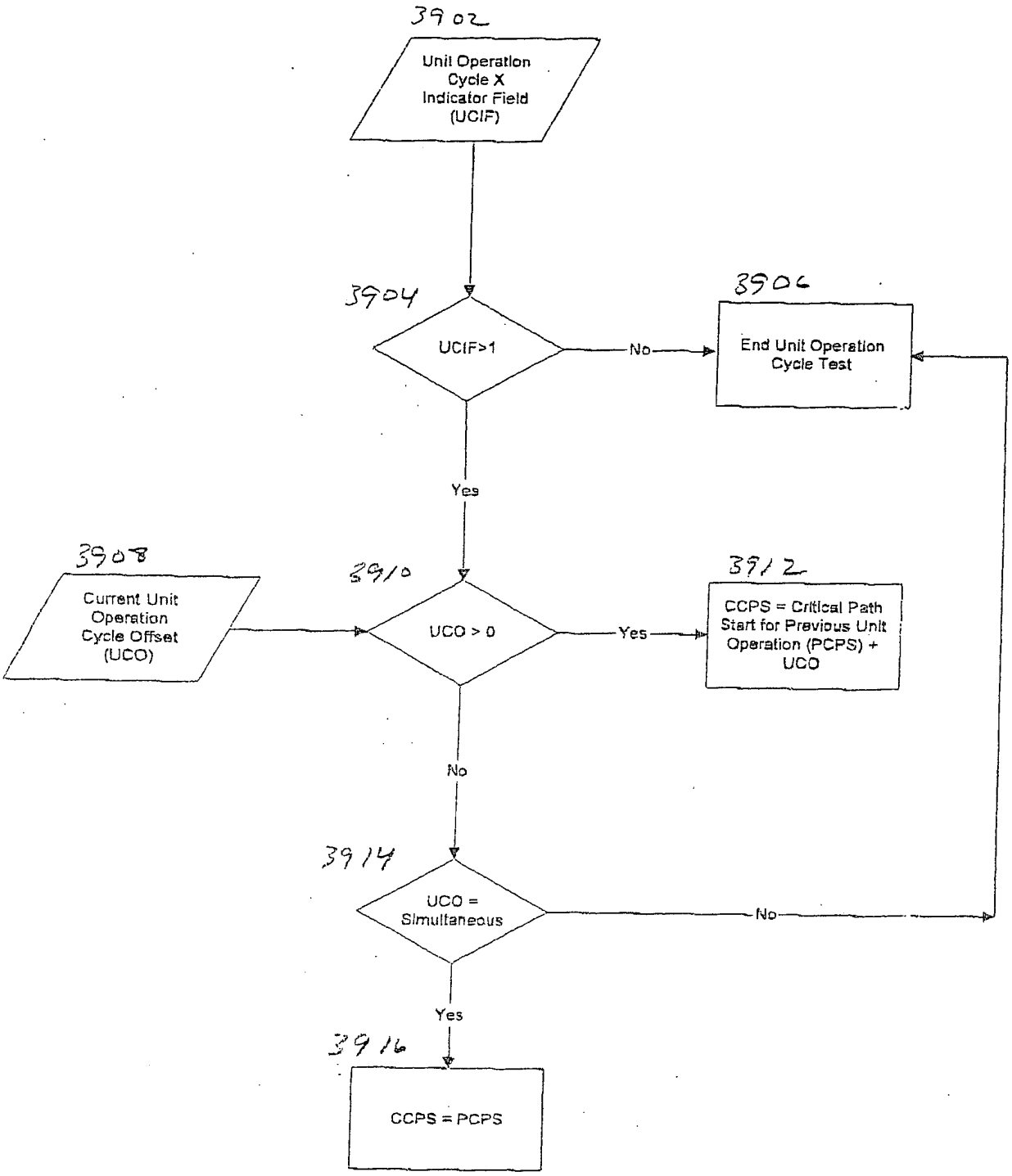

3902
Unit Operation Cycle X Indicator Field (UCIF)
3904
UCIF>1
No
3906
End Unit Operation Cycle Test
Yes
3908
Current Unit Operation Cycle Offset (UCO)
3910
UCO > 0
Yes
3912
CCPS = Critical Path Start for Previous Unit Operation (PCPS) + UCO
No
3914
UCO = Simultaneous
No
Yes
3916
CCPS = PCPS

FIG 39

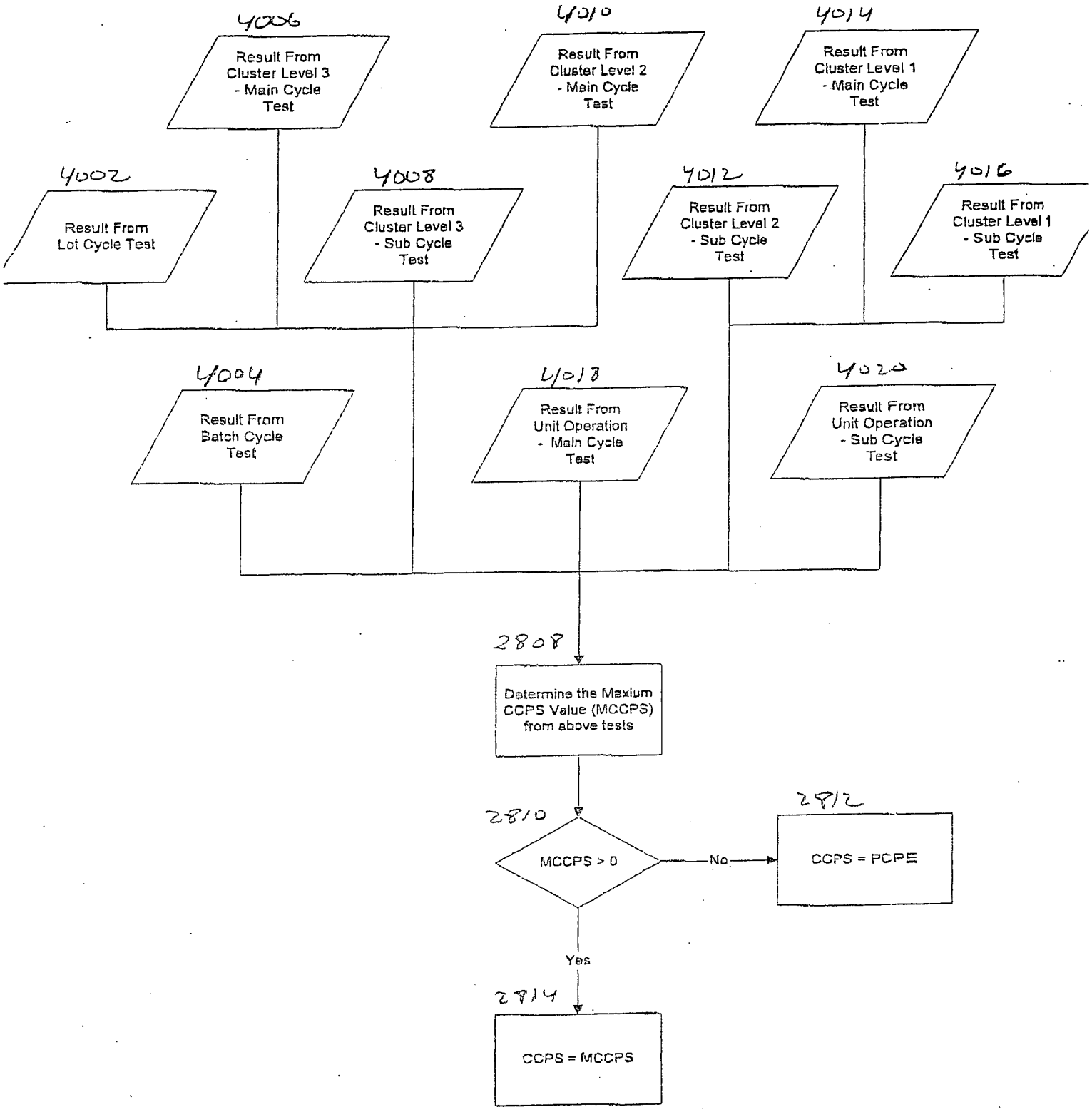

4006
Result From Cluster Level 3 - Main Cycle Test
4010
Result From Cluster Level 2 - Main Cycle Test
4014
Result From Cluster Level 1 - Main Cycle Test
4002
Result From Lot Cycle Test
4008
Result From Cluster Level 3 - Sub Cycle Test
4012
Result From Cluster Level 2 - Sub Cycle Test
4016
Result From Cluster Level 1 - Sub Cycle Test
4004
Result From Batch Cycle Test
4018
Result From Unit Operation - Main Cycle Test
4020
Result From Unit Operation - Sub Cycle Test
2808
Determine the Maxium CCPS Value (MCCPS) from above tests
2810
MCCPS > 0
No
2812
CCPS = PCPE
Yes
2814
CCPS = MCCPS

FIG 40

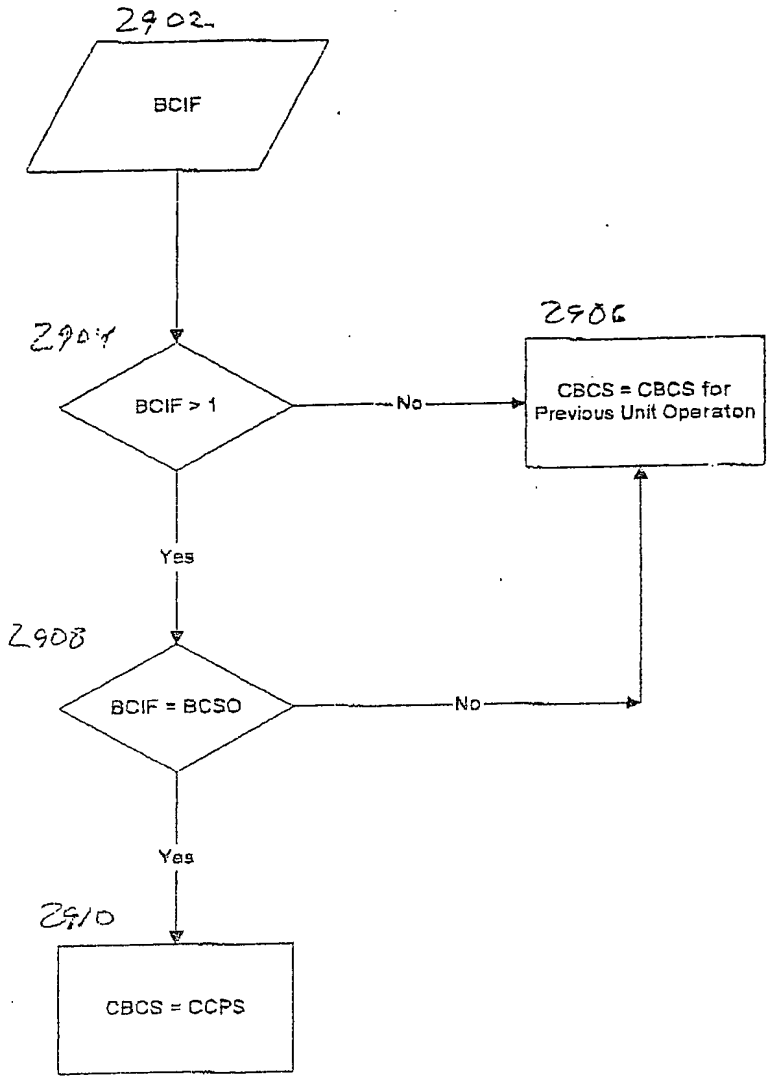

2902
BCIF
2904
BCIF > 1
No
2906
CBCS = CBCS for Previous Unit Operaton
Yes
2908
BCIF = BCSO
No
Yes
2910
CBCS = CCPS

FIG 41

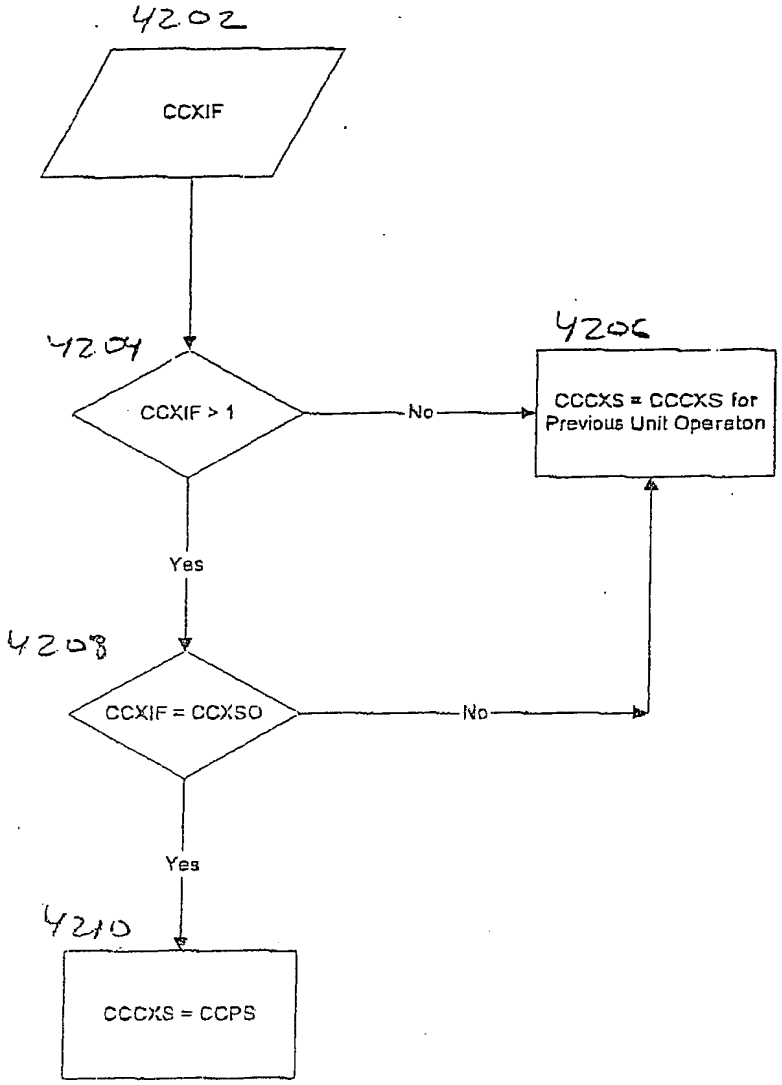

4202
CCXIF
4204
CCXIF > 1
No
4206
CCCXS = CCCXS for Previous Unit Operaton
Yes
4208
CCXIF = CCXSO
No
Yes
4210
CCCXS = CCPS

FIG 42

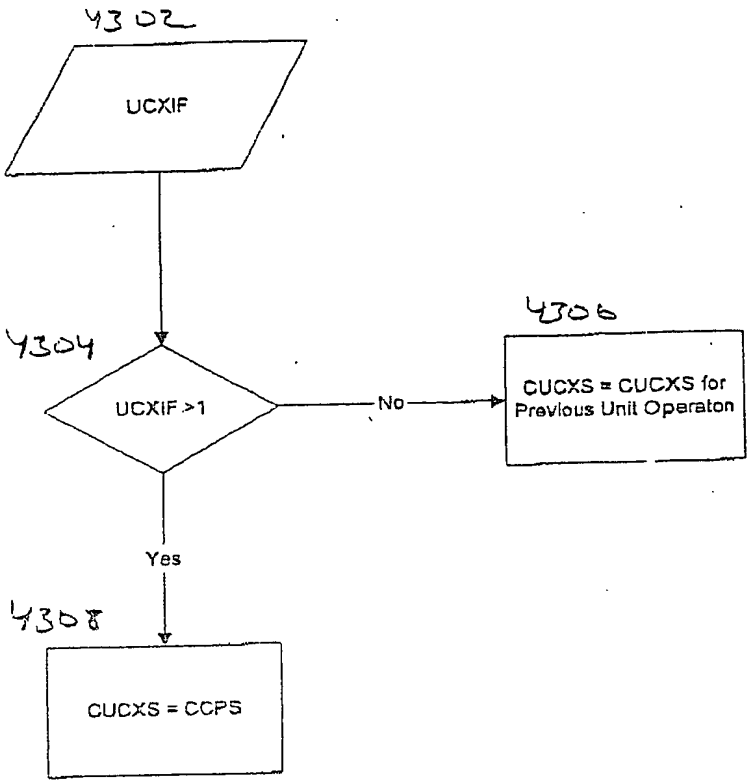

4302
UCXIF
4304
UCXIF >1
No
4306
CUCXS = CUCXS for Previous Unit Operaton
Yes
4308
CUCXS = CCPS

FIG 43

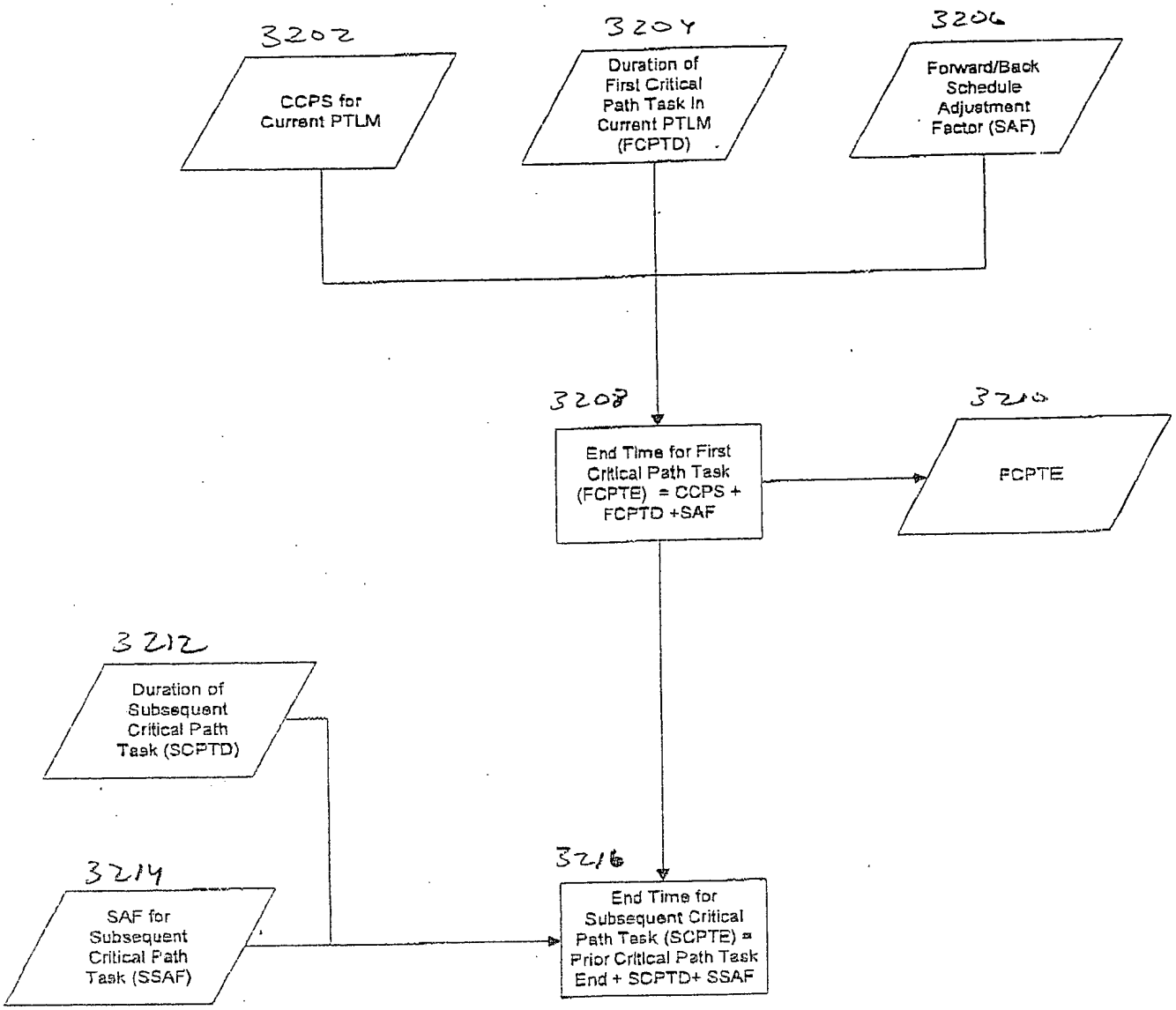

3202
CCPS for Current PTLM
3204
Duration of First Critical Path Task In Current PTLM (FCPTD)
3206
Forward/Back Schedule Adjustment Factor (SAF)
3208
End Time for First Critical Path Task (FCPTE) = CCPS + FCPTD +SAF
3210
FCPTE
3212
Duration of Subsequent Critical Path Task (SCPTD)
3214
SAF for Subsequent Critical Path Task (SSAF)
3216
End Time for Subsequent Critical Path Task (SCPTE) = Prior Critical Path Task End + SCPTD+ SSAF

FIG 44

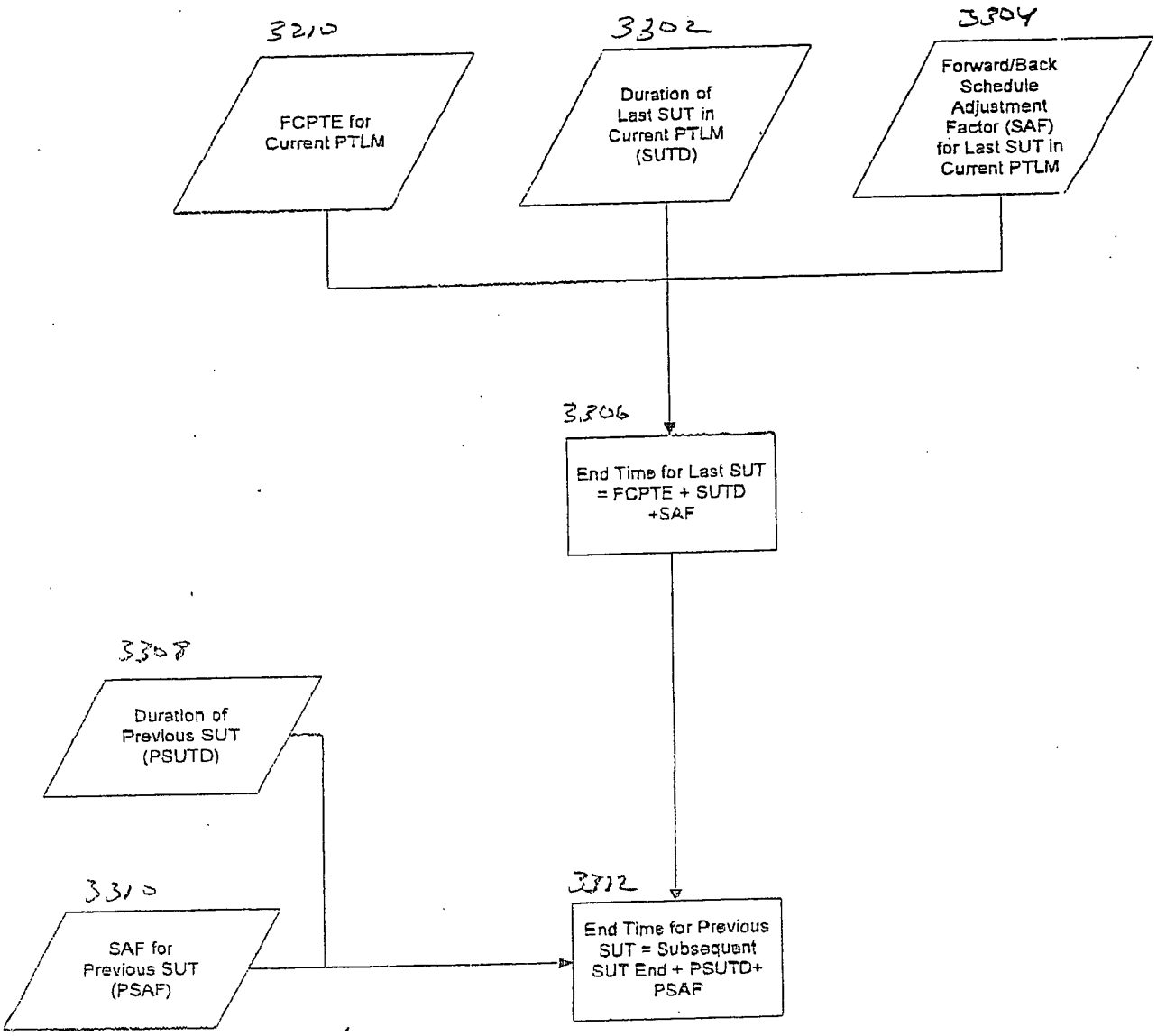

3210
FCPTE for Current PTLM
3302
Duration of Last SUT in Current PTLM (SUTD)
3304
Forward/Back Schedule Adjustment Factor (SAF) for Last SUT in Current PTLM
3306
End Time for Last SUT = FCPTE + SUTD +SAF
3308
Duration of Previous SUT (PSUTD)
3310
SAF for Previous SUT (PSAF)
3312
End Time for Previous SUT = Subsequent SUT End + PSUTD+ PSAF

FIG 45

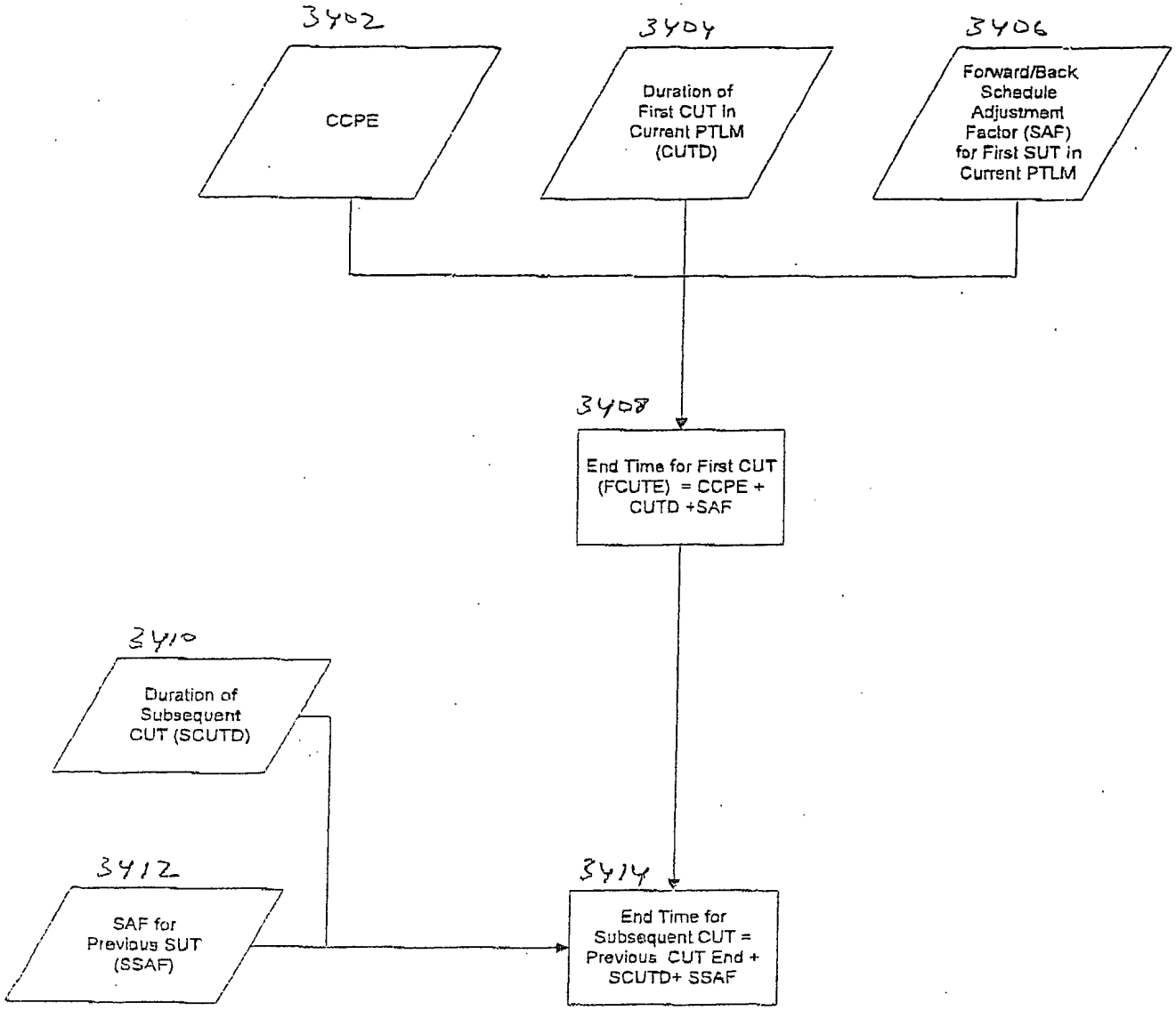

3402
CCPE
3404
Duration of First CUT In Current PTLM (CUTD)
3406
Forward/Back Schedule Adjustment Factor (SAF) for First SUT in Current PTLM
3408
End Time for First CUT (FCUTE) = CCPE + CUTD +SAF
3410
Duration of Subsequent CUT (SCUTD)
3412
SAF for Previous SUT (SSAF)
3414
End Time for Subsequent CUT = Previous CUT End + SCUTD+ SSAF

FIG 46

4702	4704	4706	4708	4710	4712	4714	4772	4774	4776	4778	4780	4782	4784	4786
							Batch Cycles/Process Cycle				Lot Cycles/Process Cycle			
	Unit Operation (APT)	Description	Code	Stage ID	Stage Inputs	Tag	Iters.	UnOp Start	UnOp End	Offset (Hrs)	Iters.	UnOp Start	UnOp End	Offset (Hrs)
	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes
	Stage 1													
1	Culture Vessel Seeding - Microcarrier Culture	Initial Seeding		1		10101	1				1			
2	Spinner Flask Split - Microcarrier Culture	Spinner Flask Split		1		10102	1				1			
3	Spinner Flask Split - Microcarrier Culture	Spinner Flask Split		1		10103	1				1			
4	Spinner Flask Split - Microcarrier Culture	Spinner Flask Split		1		10104	1				1			
5	Stirred Tank Reactor - Microcarrier Seed	20 L Seed Reactor		1		10105	1				1			
6	Stirred Tank Reactor - Microcarrier Seed	80 L Seed Reactor		1		10106	1				1			
7	Stirred Tank Reactor - Microcarrier Seed	640 L Seed Reactor		1		10107	1				1			
8	Stirred Tank Reactor - Microcarrier Seed	4,000 L Seed Reactor		1		10108	1				1			
	Stage 2				1									
9	Up Stream Multi-Stage Input			2		10201	1				1			
10	Stirred Tank Reactor - Microcarrier Preparation	Production Reactor 1		2		10202	1				1			
11	Stirred Tank Reactor - Microcarrier Production	Production Reactor 1		2		10203	1				1			
12	Harvest/Feed - Microcarrier Production			2		10204	20	10204	10315	72	10	10204	10315	144
	Stage 3				2									
13	Down Stream Multi-Stage Input			3		10301	20	10301	10315	72	10	10301	10315	144
14	Outlet Heat Exchange	Harvest Cooling to 25 C		3		10302	20	10301	10315	72	10	10301	10315	144
15	Cont. Centrifugation - Light Phase Harvest			3		10303	20	10301	10315	72	10	10301	10315	144
16	Tangential Flow - Solids Removal			3		10304	20	10301	10315	72	10	10301	10315	144
17	Prod. Ads. Chromatography - MPLC	Protein A Column		3		10305	20	10301	10315	72	10	10301	10315	144
18	Dilution 1 (LD/LP) - Batch	Viral Inactivation with HOAc		3		10306	20	10301	10315	72	10	10301	10315	144
19	Dilution 1 (LD/LP) - Batch	Adjustment to pH 8.0		3		10307	20	10301	10315	72	10	10301	10315	144
20	Microfiltration - Dead End - Solids Removal	0.45 u		3		10308	20	10301	10315	72	10	10301	10315	144
21	Microfiltration - Dead End - Solids Removal	0.2 u		3		10309	20	10301	10315	72	10	10301	10315	144
22	Cont. Ads. Chromatography - MPLC	Anion Exchange Column		3		10310	20	10301	10315	72	10	10301	10315	144
23	Ultrafiltration - Concentration/Flow Dialysis	Concentration/Buffer Exchange		3		10311	20	10301	10315	72	10	10301	10315	144
24	Microfiltration - Dead End - Solids Removal	Nanofiltration		3		10312	20	10301	10315	72	10	10301	10315	144
25	Prod. Ads. Chromatography - MPLC	Cation Exchange Column		3		10313	20	10301	10315	72	10	10301	10315	144
26	Microfiltration - Dead End - Solids Removal	0.2 u Filtration		3		10314	20	10301	10315	72	10	10301	10315	144
27	Liquid Storage			3		10315	20	10301	10315	72	10	10301	10315	144

FIG 47

Docket No.: 3714.1000-000
Title: The Use of Sub (Partial) Cycles, ...
Inventor: Peter G. Brown

4802 4804 4806 4808 4810 4812 4814 4816 4818 4820 4822

	Unit Operation (APT)	Description	Code	Stage ID	Stage Inputs	Tag	Process Design Cycles: Unit Operation Cycles/Cluster Level 1 Cycle — Main Cycles: Iters.	Main Cycles: Offset (Hrs)	Sub Cycles: Iters.	Sub Cycles: Offset (Hrs)
	Stage 1									
1	Plant Material Milling/Grinding	Grinding of Plant Material		1		10101	1		1	
	Stage 2				1					
2	DS Multi-Stage Input			2		10201	1		1	
3	Solid/Liquid Extraction	Aqueous Extraction		2		10202	1		1	
4	Dilution	Absorbant Addition		2		10203	1		1	
5	Microfiltration - Dead End - Solids Recovery	Absorbed Product Recovery		2		10204	1		1	
6	Resuspension	Dissociation of Absorbed Product		2		10205	1		1	
7	Vacuum Drying - Rotary	Vacuum Dry		2		10206	1		1	
	Stage 3				2					
11	DS Multi-Stage Input			3		10301	1		1	
12	Microfiltration - Dead End	Filter Press		3		10302	1		1	
13	Ultrafiltration - Concentration	Product Concentration		3		10303	1		1	
14	Microfiltration - Dead End - Solids Removal	Product Clarification		3		10304	1		1	
	Stage 4				4					
15	DS Multi-Stage Input			4		10401	1		1	
16	Prod. Ads. Chromatography - MPLC	Chromatography 1		4		10402	1		2	
17	Prod. Ads. Chromatography - MPLC	Chromatography 2		4		10403	1		2	
18	Ultrafiltration - Concentration/Flow Dialysis	Buffer Exchange		4		10404	1		1	
19	Prod. Ads. Chromatography - MPLC	Chromatography 3		4		10405	1		2	
20	Microfiltraiton - Dead End	Sterile Filtration		4		10406	1		1	
21	Ultrafiltration - Concentration	Product Concentration		4		10407	1		1	
22	Lyophillization	Freeze Dry		4		10408	1		1	

FIG 48A

Docket No.: 3714.1000-000
Title: The Use of Sub (Partial) Cycles, ...
Inventor: Peter G. Brown

4802 4804 4806 4808 4810 4812 4814 4816 4818 4820 4822 4824 4826 4828 4830 4832 4834 4836

	Unit Operation (APT)	Unit Operation Cluster Level 1 Cycle/Cluster Level 2 Cycle								Unit Operation Cluster Level 2 Cycles/Cluster Level 3 Cycle							
		Main Cycles				Sub Cycles				Main Cycles				Sub Cycles			
		Iters.	UnOp Start	UnOp End	Offset (Hrs)	Iters.	UnOp Start	UnOp End	Offset (Hrs)	Iters.	UnOp Start	UnOp End	Offset (Hrs)	Iters.	UnOp Start	UnOp End	Offset (Hrs)
	Stage 1																
1	Plant Material Milling/Grinding	1				1				3	10101	10304	24	1			
	Stage 2																
2	DS Multi-Stage Input	2	10201	10302	12	1				3	10101	10304	24	1			
3	Solid/Liquid Extraction	2	10201	10302	12	1				3	10101	10304	24	1			
4	Dilution	2	10201	10302	12	1				3	10101	10304	24	1			
5	Microfiltration - Dead End - Solids Recovery	2	10201	10302	12	1				3	10101	10304	24	1			
6	Resuspension	2	10201	10302	12	1				3	10101	10304	24	1			
7	Vacuum Drying - Rotary	2	10201	10302	12	1				3	10101	10304	24	1			
	Stage 3																
11	DS Multi-Stage Input	2	10201	10302	12	1				3	10101	10304	24	1			
12	Microfiltration - Dead End	2	10201	10302	12	1				3	10101	10304	24	1			
13	Ultrafiltration - Concentration					1				3	10101	10304	24	1			
14	Microfiltration - Dead End - Solids Removal					1				3	10101	10304	24	1			
	Stage 4																
15	DS Multi-Stage Input	1				1				1				1			
16	Prod. Ads. Chromatography - MPLC	1				1				1				1			
17	Prod. Ads. Chromatography - MPLC	1				1				1				1			
18	Ultrafiltration - Concentration/Flow Dialysis	1				1				1				1			
19	Prod. Ads. Chromatography - MPLC	1				1				1				1			
20	Microfiltraiton - Dead End	1				1				1				1			
21	Ultrafiltration - Concentration	1				1				1				1			
22	Lyophilization	1				1				1				1			

FIG 48B

Docket No.: 3714.1000-000
Title: The Use of Sub (Partial) Cycles, ...
Inventor: Peter G. Brown

4802 4804 4806 4808 4810 4812 4814 4816 4818 4820 4822 4824 4826 4828 4830 4832 4834 4836

	Unit Operation (APT)	Unit Operation Cluster Level 3 Cycles/Batch Cycle								Batch Cycles/Process Cycle				Lot Cycles/Process Cycle			
		Main Cycles				Sub Cycles											
		Iters.	UnOp Start	UnOp End	Offset (Hrs)	Iters.	UnOp Start	UnOp End	Offset (Hrs)	Iters.	UnOp Start	UnOp End	Offset (Hrs)	Iters.	UnOp Start	UnOp End	Offset (Hrs)
	Stage 1																
1	Plant Material Milling/Grinding	2	10101	10405	72	1				1				1			
	Stage 2																
2	DS Multi-Stage Input	2	10101	10405	72	1				1				1			
3	Solid/Liquid Extraction	2	10101	10405	72	1				1				1			
4	Dilution	2	10101	10405	72	1				1				1			
5	Microfiltration - Dead End - Solids Recovery	2	10101	10405	72	1				1				1			
6	Resuspension	2	10101	10405	72	1				1				1			
7	Vacuum Drying - Rotary	2	10101	10405	72	1				1				1			
	Stage 3																
11	DS Multi-Stage Input	2	10101	10405	72	1				1				1			
12	Microfiltration - Dead End	2	10101	10405	72	1				1				1			
13	Ultrafiltration - Concentration	2	10101	10405	72	1				1				1			
14	Microfiltration - Dead End - Solids Removal	2	10101	10405	72	1				1				1			
	Stage 4																
15	DS Multi-Stage Input	2	10101	10405	72	1				1				1			
16	Prod. Ads. Chromatography - MPLC	2	10101	10405	72	1				1				1			
17	Prod. Ads. Chromatography - MPLC	2	10101	10405	72	1				1				1			
18	Ultrafiltration - Concentration/Flow Dialysis	2	10101	10405	72	1				1				1			
19	Prod. Ads. Chromatography - MPLC	2	10101	10405	72	1				1				1			
20	Microfiltralton - Dead End	1				1				1				1			
21	Ultrafiltration - Concentration	1				1				1				1			
22	Lyophilization	1				1				1				1			

FIG 48C

4902	4904	4906	4908	4910	4912	4914	4956	4958	4960	4962	4964	4966	4968	4970
							Unit Operation Cluster Level 3 Cycles/Batch Cycle							
							Main Cycles				Sub Cycles			
	Unit Operation (APT)	Description	Code	Stage ID	Stage Inputs	Tag	Iters.	UnOp Start	UnOp End	Offset (Hrs)	Iters.	UnOp Start	UnOp End	Offset (Hrs)
	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes	Notes
	Stage 1													
1	1 Inoculum Preparation	0.4L		1		10101	1				1			
2	53 Microbial - Stirred Tank Reactor- Seed Fermentation	4L		1		10102	1				1			
3	53 Microbial - Stirred Tank Reactor- Seed Fermentation	40L		1		10103	1				1			
4	53 Microbial - Stirred Tank Reactor- Seed Fermentation	400L		1		10104	1				1			
5	3 Microbial - Stirred Tank Reactor - Production Fermentation	4000L		1		10105	1				1			
	Stage 2				1									
6	76 Down Stream Multi-Stage Input			2		10201	1				1			
7	51 Outlet Heat Exchange	Harvest Cooling to 4 C		2		10202	1				1			
8	26 Cont. Centrifugation - Heavy Phase Harvest	Whole Cell Harvest		2		10203	1				1			
9	47 Dilution 1 (LD/LP) - Batch	Cell Resuspension		2		10204	1				1			
10	61 Inlet Heat Exchange	Slurry Cooling to 4 C		2		10205	3	10205	10207		2	10205	10207	
11	31 High Pressure Homogenization	Cell Disruption		2		10206	3	10205	10207		2	10205	10207	
12	61 Inlet Heat Exchange	Slurry Cooling to 4 C		2		10207	3	10205	10207		2	10205	10207	
13	26 Cont. Centrifugation - Heavy Phase Harvest	IB Recovery		2		10208	1				1			
14	47 Dilution 1 (LD/LP) - Batch	IB Wash		2		10209	2	10209	10210		1			
15	26 Cont. Centrifugation - Heavy Phase Harvest	IB Recovery		2		10210	2	10209	10210		1			
16	47 Dilution 1 (LD/LP) - Batch	Solubilization		2		10211	1				1			
17	27 Cont. Centrifugation - Light Phase Harvest	Clarification		2		10212	1				1			
18	47 Dilution 1 (LD/LP) - Batch	Renaturation		2		10213	1				1			
19	34 Tangential Flow - Solids Removal			2		10214	1				1			
20	62 Ultrafiltration - Concentration/Flow Dialysis	Concentration/Buffer Exchange		2		10215	1				1			
	Stage 3				2									
21	76 Down Stream Multi-Stage Input			3		10301	1				1			
22	39 Prod. Ads. Chromatography - MPLC	Cation Exchange Column		3		10302	1				1			
23	39 Prod. Ads. Chromatography - MPLC	HIC Column		3		10303	1				1			
24	39 Prod. Ads. Chromatography - MPLC	Anioin Exchange Column		3		10304	1				1			
25	47 Dilution 1 (LD/LP) - Batch	Viral Inactivation with HOAc		3		10305	1				1			
26	47 Dilution 1 (LD/LP) - Batch	Adjustment to pH 8.0		3		10306	1				1			
27	35 Microfiltration - Dead End - Solids Removal	0.45 u		3		10307	1				1			
28	35 Microfiltration - Dead End - Solids Removal	0.2 u		3		10308	1				1			
29	35 Microfiltration - Dead End - Solids Removal	Nanofiltration		3		10309	1				1			
30	62 Ultrafiltration - Concentration/Flow Dialysis	Concentration/Buffer Exchange		3		10310	1				1			
31	39 Prod. Ads. Chromatography - MPLC	HIC Column		3		10311	1				1			
32	35 Microfiltration - Dead End - Solids Removal	Sterile Filtration		3		10312	1				1			
33	52 Liquid Storage			3		10313	1				1			

FIG 49